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Medical nutritional therapy for renal transplantation in the COVID-19 pandemic

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Abstract

Nutritional therapy is very important at renal transplantation. Nutrition has become more vital for transplantation patients owing to the coronavirus disease 2019 (COVID-19) pandemic. Inadequate nutrition can negatively affect the immune system. For this reason, adequate protein and energy intake should be provided to the patients. Also, overconsumption of saturated fat, sugar, and refined carbohydrates can both negatively affect the immune system and trigger chronic diseases in transplantation patients. In addition, vitamins and minerals should be monitored and inadequacy should be prevented due to immunomodulatory effects. Applying nutritional therapy suitable for the symptoms of renal transplantation patients and preventing comorbidities may reduce the risk and severity of COVID-19 infection.

Key Words: Nutrition; Renal transplantation; COVID-19

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Core Tip: Before and after renal transplantation, recipient patients are in the risk group for the coronavirus disease 2019 pandemic. Therefore, adequate energy and nutrient requirements should be provided and nutritional therapy should be planned according to the symptoms of the patients.

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**INTRODUCTION**

Renal transplantation is a renal replacement therapy that improves long-term survival, quality of life, and uremia and metabolic abnormalities[1]. Medical nutritional therapy is of great importance in patients before and after transplantation. Medical nutritional therapy is defined as “nutritional diagnostic, therapy, and counseling services for the purpose of disease management, which are furnished by a registered dietitian or nutrition professional” by United States Department of Health and Human Services [2]. This therapy can prevent many risk factors, including body weight gain, high blood pressure, dyslipidemia, and diabetes[3]. Especially after transplantation, the nutritional behavior of patients can be negatively affected in the long term. Generally, increases in protein, saturated fat, sugar, and salt intake occurred[4]. Post-transplantation obesity increases the risk of graft failure and mortality[1]. Therefore, specially planned nutritional treatments should be applied for specific complications, immunosuppression effects, and electrolyte imbalances in transplantation patients[3].

The coronavirus pandemic that emerged in 2019-coronavirus disease 2019 (COVID-19) still continues to affect the world. The mortality rate from this disease is higher in the elderly and those with comorbidities[5,6]. End-stage renal disease awaiting renal transplantation and renal transplantation patients are in the risk group for the COVID-19 pandemic. It appears that these patients are more likely to infected COVID-19 and the recovery process is more difficult. Therefore, nutrition becomes more important to protect the immune system in these patients[7].

In this review, it is aimed to emphasize the importance of nutritional therapy in renal transplantation patients in the COVID-19 pandemic.

RENAL TRANSPLANTATION AND COVID-19

Body weight gain is a common condition seen in patients after renal transplantation. Steroids, immunosuppressive drugs, and elimination of chronic disease are thought to be the cause of this condition. With fewer dietary restrictions and increased appetite, patients' eating habits change and patients get more energy[8]. Increased appetite and metabolic changes after successful renal transplantation can lead to risks if not regulated by nutritional interventions[9]. Excessive body weight can increase mortality and morbidity due to hypertension, dyslipidemia, diabetes, and cardiovascular diseases[8]. In all these cases, nutrition may be an appropriate intervention for the management or prevention of chronic diseases[9].

COVID-19 infection may be more severe in renal transplantation patients. Recipients usually receive an immunosuppressive treatment protocol after the transplantation. Prolonged immunosuppression is associated with an increased risk of infectious complications, and ribonucleic acid is more susceptible to infections from respiratory viruses[7]. In most patients with COVID-19, supportive treatment is applied to the patient by reducing the suppression of immunity[10]. However, it is observed that patients are treated without interruption or reducing immunosuppressive therapy[11].

Obesity, especially in the post-transplantation stage, poses a risk for COVID-19. Obesity is considered a risk factor for comorbidities and deterioration of the metabolic state and is associated with an increased risk of pneumonia[12,13]. Some studies indicated higher prevalence of obesity in individuals who are dependent on mechanical ventilation due to COVID-19[14,15]. The relationship between renal transplantation, chronic diseases, and COVID-19 is given in **Figure 1**.

NUTRITIONAL THERAPY BEFORE RENAL TRANSPLANTATION

While waiting for transplantation, the nutritional status of the patients may deteriorate due to various reasons such as reduced food intake and dietary restrictions. Nutrition should be improved and nutritional status should be optimized before renal transplantation. Before transplantation, nutritional therapy helps to increase energy intake and prevent fat and muscle loss. In addition, nutritional status is positively associated with successful transplantation and survival in patients. Therefore, maintenance of optimal nutritional status, including body composition, should be ensured in all patients with end-stage renal disease[16,17].

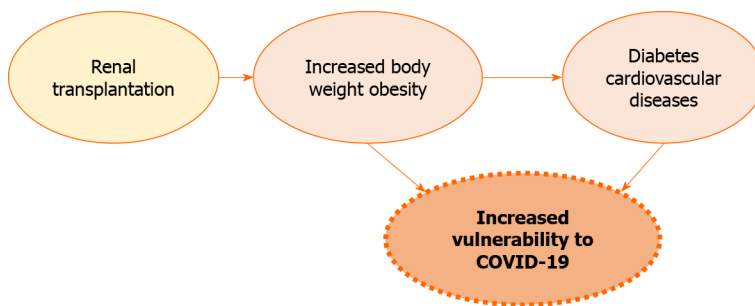


Figure 1 Renal transplantation, chronic diseases and coronavirus disease 2019.

Malnutrition, inadequate sleep, psychosocial or physical stress can endanger the body's immune system. During active COVID-19 infection, it is recommended to reduce and prevent the risk of protein-energy wasting (PEW) in all patients with kidney disease. It is thought that adequate protein and energy intake can prevent or improve hypokalemia, hypophosphatemia, PEW, sarcopenia, and cachexia[18,19].

In addition to nutrition, patients with end-stage renal diseases are advised to follow masks, distancing and hygiene rules as much as possible, and even avoid personal contact with family members. These recommendations should be followed by renal transplantation recipients during and after hospitalization[20].

NUTRITIONAL THERAPY AFTER RENAL TRANSPLANTATION

Early post transplantation nutritional goals include preventing catabolism, promoting wound healing, improve electrolyte imbalances, and maintaining blood glucose control. The side effects of immunosuppression in the late period after transplantation are increased bodyweight, which can be explained by sedentary lifestyle, food intake, and appetite. In post transplantation nutrition therapy, it should be aimed to balance electrolyte changes and to minimize the risk of osteoporosis and cardiovascular disease[16]. The COVID-19 pandemic has brought some concerns and changes in the nutritional treatments of renal transplantation patients, who are a risky group. European Society for Clinical Nutrition and Metabolism (ESPEN) recommends malnutrition screening, providing nutritional counseling and micronutrient supplementation in patients with malnutrition, and regular physical activity in quarantine, in COVID-19 nutrition guideline[21].

Energy and protein

The focus should be on optimizing nutrition for the patient in the early period after transplantation and adequate nutrition should be provided. Even if the patient is obese in the early period after transplantation, weight loss should not be the goal. Therefore, 30-35 kcal/kg/d for dietary energy and 1.2-2.0 g/kg/d for protein are recommended in the early period. In the long term after transplantation, dietary recommendations should not differ significantly from the general population, unless there is another underlying problem. Long-term energy recommendations offer a wide range of 23-35 kcal/kg/d and should aim to maintain a healthy body weight[9]. National Kidney Foundation 2020 Guidelines recommend 25-35 kcal/kg/d energy intake for post transplantation patients[22]. Protein recommendations in the long term after transplantation vary depending on the diabetes status. While the protein recommendation for a patient without diabetes is 0.6-0.8 g/kg/d, protein recommendation for a patient with diabetes is 0.8-0.9 g/kg/d[9]. The reason why the protein recommendation is high immediately after transplantation is the ability to reverse the negative nitrogen balance[23].

COVID-19 and its symptoms can cause a loss of appetite and increase the risk of malnutrition. Energy and protein recommendations for patients with COVID-19 are similar to early post transplantation recommendations[19,24,25]. Nutritional therapy for patients after renal transplantation is given in Figure 2.

Fat and carbohydrate

Consumption of a healthy diet should be emphasized due to the risk of excessive weight gain in patients with renal transplantation. Excessive body weight gain brings

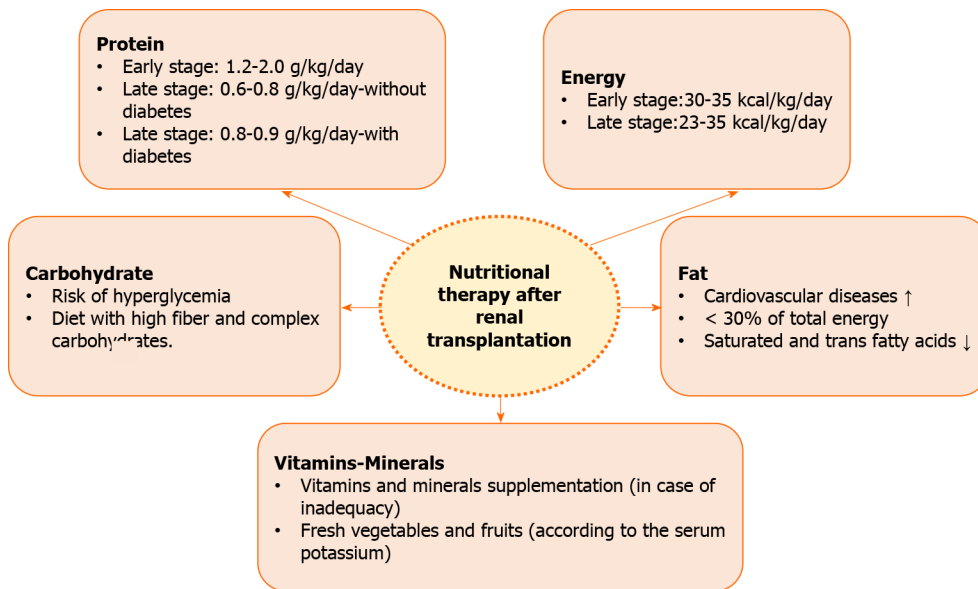


Figure 2 Nutritional therapy after renal transplantation.

with it other potential obesity-related comorbidities such as diabetes, hypertension, hyperlipidemia and cardiovascular disease. Intervention should be initiated immediately after transplantation to reduce the impact of these comorbidities[16]. The goal should be to control blood lipids through diet by consuming < 30% of total calories from fat per day. It is important to emphasize the intake of monounsaturated and polyunsaturated fat, low saturated fat, and minimal trans-fat[9].

After transplantation, the use of high doses corticosteroids and wound healing is a very important issue. In addition, the stress caused by surgery can trigger hyperglycemia. High serum glucose levels increase the risk of bloodstream infections, delay wound healing, and can trigger oxidative stress[3]. For this reason, the intake of high fiber, whole grain and complex carbohydrate is recommended for patients after transplantation. Carbohydrates should provide 50%-70% of non-protein energy in the early period after transplantation. However, this rate should be reduced to 45%-50% of total energy in the long term after transplantation[9].

Diets that include excessive consumption of sugar, saturated fat, and refined carbohydrates are known to negatively affect the immune system and these diets can exacerbate the problems caused by COVID-19. Healthy eating habits should be considered to reduce susceptibility to COVID-19 and long-term complications[26].

Vitamin and minerals

Long-term steroid use in renal transplantation patients and renal dysfunction in pre-transplantation period may have adverse effects on bone health[9]. Kidneys are involved in balancing some electrolytes and micronutrients. Therefore, problems with phosphorus, magnesium, and vitamin D may arise in transplantation patients[3]. Supplementations of calcium, vitamin D, magnesium, and phosphorus are recommended if needed[9,22].

The use of vitamin D seems beneficial in preventing the risk of bone fractures. A combination of these agents, rather than a single agent, can significantly reduce the risk of bone fracture in preventing the risk of bone loss. Hypophosphatemia is a common complication after renal transplantation. For this reason, it is recommended to provide 1200-1500 mg of phosphorus intake per day[16].

Micronutrients play a dominant role in immunomodulation. The deficiency of most nutrients increases susceptibility to viral infection. The primary defense against the virus is the protection of the physical and biochemical barriers of the respiratory tract. Vitamins and minerals have many important roles such as epithelial differentiation and growth, preservation of membrane fluidity and integrity, reduction of membrane lipid peroxidation, regulation of antimicrobial peptide activities, and regulation of immune cells[27,28]. Principally, low levels of some micronutrients have been associated with negative clinical outcomes during viral infections[21]. Vitamins A, D, B, C, omega-3, as well as selenium, zinc and iron should be advised in the assessment of micronutrients in COVID-19 patients[29]. During infections, micronutrients may

decrease in the body. Therefore, supplementations can help restore normal blood levels. Regarding supplements, it is not recommended for use without the advice of a healthcare professional, as these supplementations may interact with other nutrients, medications, and medical treatments[19].

Vitamin D, which is also important for renal transplantation patients, is also prominent in the COVID-19 pandemic due to its anti-inflammatory effects[6,30]. In response to COVID-19 infection, vitamin D can prevent disease progression through the production of antimicrobial peptides in the respiratory epithelium and help reduce inflammatory response[31]. Vitamin D deficiency has been reported to increase the rate of hospitalization and mortality due to COVID-19[32].

Vitamin C is an important antioxidant nutrient, specifically for white blood cells to fight infections. Vitamin C contributes to immunity by supporting both the innate and adaptive immune system, modulating inflammatory mediators, and influencing epithelial barriers. It has important benefits such as preventing common cold and upper respiratory tract infections, reducing the duration and severity of the disease and supporting respiratory defense mechanisms[31]. In addition, it is thought that vitamin C may have a positive effect against COVID-19, as many upper respiratory tract infections are caused by endemic coronaviruses[33]. In excessive intake of Vitamin C, accumulation of oxalose, which is a metabolic byproduct of ascorbic acid, can be seen in kidney patients. Therefore, dietary vitamin C intake appears to be safer than supplementation[31]. Consumption of fresh vegetables and fruits with high vitamin C contributes to increasing the intake of not only vitamin C but also other antioxidant vitamins. However, it should not be forgotten that the potassium contents of vitamin C sources are generally high. Therefore, it is important to offer these recommendations by monitoring serum potassium levels in patients[18].

Iron deficiency and related anemia are frequently seen in renal transplantation patients due to insufficient iron stores, intraoperative blood loss and frequent phlebotomy after transplantation. During the first 12 wk after transplantation, blood and iron losses are important and may require intravenous iron administration[34]. Although iron supplementation offers immune-boosting benefits in individuals with iron deficiency, it can exacerbate infections and inflammation. Given that iron is important for viral replication, the safety and effectiveness of iron supplementation during the COVID-19 pandemic is controversial[35].

Nutraceuticals can increase the immune responses of people infected with encapsulated RNA viruses such as influenza and coronavirus. Because of the immune-modulating effects of nutraceuticals such as beta-glucans, melatonin and probiotics, it might be valuable for efficient clinical outcomes for COVID-19 patients. However, there are insufficient data and strong evidence for these components[31,36].

Nutritional support

Nutritional support is recommended for patients who cannot or are predicted to be unable to meet their energy and nutrient requirements sufficiently before and after transplantation. In the post transplantation period, oral food intake and enteral nutrition are recommended as early as possible. The use of standard enteral formulas is generally recommended for the patients. However, the use of renal enteral formulas comes to the fore in patients with electrolyte disturbances in the early period after transplantation[37,38]. Similarly, in polymorbid intensive care patients with COVID-19, oral nutritional supplements are recommended in patients who are not intubated. If the patient is intubated, post-pyloric nasogastric tube feeding can be suggested. Parenteral nutrition is recommended for patients whose energy and nutrient intake is insufficient through oral nutritional supplements and tube enteral nutrition or who are contraindicated for enteral nutrition[21]. It is observed that enteral formulas with moderately high protein are generally recommended for patients with COVID-19. This recommendation seems more applicable in patients who received dialysis treatment before renal transplantation. If there is no electrolyte disorder in patients with COVID-19 in the post transplantation, it may be more appropriate to use standard isoosmolar polymeric enteral formulas[39-42]. In addition, it is thought that products enriched with omega-3 fatty acids, which have a positive effect on kidney functions, can both improve oxygenation and help reduce especially cardiovascular complications of COVID-19[21,43].

Other recommendations

Renal transplantation patients are affected by more morbidity and mortality due to the increased prevalence of cardiovascular risk factors[44]. Bodyweight gain and obesity are common conditions during the first year after renal transplantation[16]. A healthy lifestyle and physical activity are recommended to improve this condition. It is

recommended that a minimum 30 min of moderate-intensity physical activity five times a week for patients with chronic kidney disease[44]. The physical activity recommendation of ESPEN in the COVID-19 guideline is similar to this recommendation. This guideline recommends every day > 30 min or every second day > 1 h exercise to maintain fitness, mental health, muscle mass and therefore energy expenditure and body composition[21]. Physical activity before and after renal transplantation is low, and this may be associated with rejection[44]. Due to the COVID-19 pandemic, patients should be advised to eat a healthy diet and stay physically active in addition to personal hygiene and physical distance recommendations[6,45].

CONCLUSION

As a result, medical nutritional therapy plays an important role in renal transplantation patients. Appropriate nutritional intervention helps to reduce rejection and comorbid risk factors. Because of the COVID-19 pandemic, these patients are in the risk group. Applying nutritional therapy suitable for the special conditions of renal transplantation patients and preventing comorbidities may decrease the risk and severity of COVID-19 infection. Therefore, routine follow-up with a dietician is recommended to maintain nutritional motivation and achieve optimum results.

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