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Frailty syndrome in patients with chronic kidney disease

Síndrome de debilidad en pacientes con enfermedad renal crónica

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SUMMARY

Due to the increase in life expectancy and the number of elderly people, the prevalence of age-related diseases, including frailty syndrome, is growing. **Objective:** *The study aims to investigate the features and characteristics of frailty syndrome in patients with chronic kidney disease.* **Method:** *Literature was sourced from PubMed, Embase, Scopus, Google Scholar, and Web of Science. The available published studies from 2015 to 2024 were examined and analyzed in detail. Frailty syndrome was found to be diagnosed in 60 % of patients with chronic kidney disease, mostly in stages 3-5.* **Results:** *Frailty syndrome is most common among the elderly. At the same time, among young patients undergoing dialysis treatment, the prevalence of frailty syndrome is 35 %. The main symptoms of the above pathology are unintentional weight loss, subjective feelings of fatigue and exhaustion, feelings of weakness and reduced physical activity, slow walking speed, and decreased muscle strength. The following diagnostic methods are effective: the Fried and Clinical Weakness Scales. The treatment, prevention, and rehabilitation of frailty syndrome are based on eating healthy food, exercising, and having an active social life. This helps to extend the period of independence of patients, reduces the risk of falls and fractures, improves balance and cognitive function, reduces stress and anxiety, and improves overall quality of life. The results of this study can be used to develop effective methods for the prevention and rehabilitation of frailty in patients with chronic kidney disease.*

Keywords: *Fatigue, decreased muscle strength, hemodialysis, risk of falling, Fried's scale.*

RESUMEN

Debido al aumento de la esperanza de vida y al número de personas mayores, está aumentando la prevalencia de enfermedades relacionadas con la edad, incluido el síndrome de fragilidad. **Objetivo:** *El estudio tiene como objetivo investigar los rasgos y características del síndrome de fragilidad en pacientes con enfermedad renal crónica.* **Método:** *La literatura se obtuvo de PubMed, Embase, Scopus, Google Scholar y Web of Science. Se examinaron y analizaron en detalle los estudios publicados disponibles entre 2015 y 2024. Se encontró que el síndrome de fragilidad se diagnosticaba en el 60 % de los pacientes con enfermedad renal crónica, principalmente en las etapas 3-5.* **Resultados:** *El síndrome de fragilidad es más común entre los ancianos. Al mismo tiempo, entre los pacientes jóvenes en tratamiento de diálisis, la prevalencia del síndrome de fragilidad es del 35 %. Los principales síntomas de la patología anterior son pérdida de peso involuntaria, sensación subjetiva de fatiga y agotamiento, sensación de debilidad y*

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reducción de la actividad física, lentitud al caminar y disminución de la fuerza muscular. Los siguientes métodos de diagnóstico son eficaces: la escala de debilidad de Fried y la escala de debilidad clínica. El tratamiento, prevención y rehabilitación del síndrome de fragilidad se basan en una alimentación saludable, ejercicio y una vida social activa. Esto ayuda a prolongar el período de independencia de los pacientes, reduce el riesgo de caídas y fracturas, mejora el equilibrio y la función cognitiva, reduce el estrés y la ansiedad y mejora la calidad de vida en general. Los resultados de este estudio se pueden utilizar para desarrollar métodos eficaces para la prevención y rehabilitación de la fragilidad en pacientes con enfermedad renal crónica.

Palabras clave: *Fatiga, disminución de la fuerza muscular, hemodiálisis, riesgo de caídas, escala de Fried.*

INTRODUCTION

Chronic kidney disease (CKD) is a widespread problem of global importance. This is related to the increase in life expectancy and the emergence of a significant number of medications whose side effects include damage to the nephron structure and changes in kidney function. The prevalence of this disease is about 11 %-16 % of Poland's population (1-2). As chronic kidney disease progresses, changes in metabolism and normal kidney function occur, and chronic inflammation, metabolic acidosis, accumulation of uremic toxins, endocrine disorders, and anorexia develop (3). Haemodialysis stimulates protein catabolism and slows down its anabolism, which leads to a decrease in muscle mass and strength. These factors lead to the development of frailty syndrome. The main problem is that frailty syndrome is a multifactorial disease. In older people with numerous chronic diseases, it is often impossible to identify the root cause of this pathology. This significantly complicates diagnosis and, accordingly, reduces the effectiveness of treatment. The presence of frailty in patients with CKD is associated with an unfavorable prognosis for falls, hospitalization, quality of life, and mortality. This syndrome has been described in 60 % of people with end-stage CKD (most common among patients with stage 3-5 chronic kidney disease).

Frailty syndrome is often diagnosed in older people. The incidence in Europe ranges from 6.% to 27 %, and in Poland it is about 3 % (1-2). At the same time, it is worth noting that young patients who have been treated since childhood for renal diseases also have a high risk of developing frailty syndrome despite their young age. This significantly worsens such patients' quality of life and increases the healthcare system's economic burden. Kaczorowska et al. (2) assessed physical fitness and analyzed the risk factors for frailty syndrome among older people. However, this study did not consider a sample of young and middle-aged patients. Zawadzki et al. (4) studied the peculiarities of iron metabolism in patients with a history of frailty syndrome. However, the study's limited generalizability may result from its narrow regional emphasis and relatively small sample size. Furthermore, although the study shows a connection between low iron levels and frailty syndrome, it does not prove causation. Michalik et al. (5) investigated the prevalence of frailty syndrome in urological patients who underwent surgery due to the development of malignant disease. This underscores the significance of doing a comprehensive geriatric assessment (CGA) to detect signs of frailty. However, the reliability and validity of widely used frailty screening measures in this cohort are called into question, given the notable difference between the frailty prevalence determined by CGA (39.7 %) and screening tests (4.4 %-10.3 %).

Bąk et al. (6) studied the impact of frailty syndrome on the quality of life and symptoms of depression in people with type 2 diabetes mellitus. The cross-sectional design of the study, nevertheless, restricts our ability to comprehend the causal connections between depression, diabetes, and frailty. The study may also be biased because it relies on self-reported assessments of depression symptoms and quality of life. Talha et al. (7) estimated the prevalence of frailty syndrome among patients with heart failure. However, these studies did not describe patients with chronic kidney disease. Rolf et al. (8) studied the relationship between nutritional quality and frailty syndrome in elderly patients. The study's relatively small sample size and the lack of information provided by the authors regarding the sample's representativeness of the broader aged population may restrict the

generalizability of the results. It is worth noting that the above studies focused on elderly patients, but frailty syndrome is common among patients with CKD of any age.

Therefore, the study aims to analyze the prevalence and characteristics of frailty syndrome in patients with chronic kidney disease of different age groups and provide up-to-date information on risk factors, pathogenesis, symptoms, diagnosis, treatment, prevention, and rehabilitation of frailty syndrome.

MATERIALS AND METHODS

A thorough systematic search of relevant data on frailty syndrome in patients with chronic kidney disease of different age groups was carried out to perform this theoretical study. The necessary information was collected in the following databases: PubMed, Embase, Scopus, Google Scholar, and Web of Science. The published papers from 2015 to 2024 in peer-reviewed journals in Polish, French, English, and Spanish were studied and analyzed in detail. The necessary data was searched using a combined set of keywords: "chronic kidney disease," "epidemiology of chronic kidney disease," "prevention of chronic kidney disease," "rehabilitation of chronic kidney disease," "treatment of chronic kidney disease," "frailty syndrome," "prevalence of frailty syndrome," "risk factors for frailty syndrome," "symptoms of frailty syndrome," "pathogenesis of frailty syndrome," "diagnostic criteria for frailty syndrome," "treatment of frailty syndrome," "rehabilitation of frailty syndrome," "prevention of frailty syndrome," "fatigue," "risk of falling," "loss of muscle strength," "ageing population," "haemodialysis," "dialysis," "nephron," "chronic inflammation," "metabolic acidosis," "Fried's Weakness Scale," "clinical frailty scale".

All relevant articles were found and reviewed: clinical trials, randomized controlled trials, reviews, systematic reviews, and meta-analyses. The publications were carefully reviewed and selected by title, abstract, relevance to the topic, and appropriate level of evidence for the case studies. The existing reference lists for the relevant articles were analyzed to find other additional and relevant studies, and their contents were carefully reviewed. The following information was extracted from the list of papers identified: basic information about the study, all authors and their contributions, the period of publication and the region where the study was conducted, information about the size of the study sample, and the period of follow-up. After removing duplicates and checking the titles and abstracts, the papers were assessed according to the existing inclusion and exclusion criteria.

The presented theoretical work includes studies that reported on the features of the course, epidemiology, risk factors, symptoms, diagnosis, treatment, prevention, and rehabilitation of frailty syndrome in people with chronic kidney disease. Studies describing in detail the pathogenetic features of frailty syndrome in various pathologies (chronic kidney disease, cardiovascular failure, diabetes mellitus, and endocrine disorders) and natural aging were selected and included. Papers describing the peculiarities of the course of frailty syndrome in the setting of chronic kidney disease in people of different age groups (young, middle-aged, and elderly) were included. The articles were excluded in the following cases: the information presented was outdated and irrelevant, there were doubts about the reliability of the experiment and the results of the study, and the experiment was conducted on animals.

After a thorough selection process, 45 relevant studies with relevant information were identified. The results of the selected studies are cited in this paper in compliance with all requirements and copyrights.

RESULTS AND DISCUSSION

Etiology and pathogenesis of frailty syndrome in patients with CKD

Frailty syndrome is a clinical syndrome characterized by a decrease in adaptive and physiological reserve and increased susceptibility to stress factors (various diseases, injuries) resulting from progressive and continuous degeneration of the physiological systems of the human body, including disorders of the endocrine and immune systems (9). The etiology

of frailty syndrome in patients with CKD is multifactorial. Hormonal, immunological, and metabolic changes, such as metabolic acidosis, electrolyte disorders, malnutrition, and impaired oxygen transport due to anemia, affect the onset and development of the pathology (9). Among patients with kidney disease, the highest risk of developing frailty syndrome is among people on dialysis treatment (about 41 %), and the lowest risk is among kidney transplant recipients (about 21 %).

Progression of chronic kidney disease leads to decreased appetite, decreased food intake, anorexia caused by uremic toxins and other anorexigenic (tumor necrosis factor-*a*, cholecystokinin, leptin), taste/smell disturbances, and inflammation. Loss of protein and amino acids from the dialysis fluid develops, especially in peritoneal dialysis; loss of protein in the urine and high proteinuria in the event of nephrotic syndrome. As a result of the breakdown processes, the concentration and activity of catabolic hormones increase: parathyroid hormone, glucagon, corticosteroids, and angiotensin II. Deficiency or resistance to anabolic hormones develops insulin, growth hormone, insulin-like growth factor 1 (IGF-1), testosterone, 25(OH)D_3, or 1,2-dihydroxy cholecalciferol. Metabolic acidosis activates the caspase-3 and ubiquitin-proteasome systems in skeletal muscle, promoting protein breakdown and inhibiting protein synthesis. Primary neuromuscular disorders, central nervous system dysfunction, specific neural changes, dementia, peripheral nervous system dysfunction, myocyte loss, reduction in the number of satellite cells and myogenic factors, and tendon stiffness develop. There is a violation of apoptosis, an increase in the number of senescent cells, a decrease in cellular replenishment by stem cells, a reduction in autophagy, and a disruption of the process of deoxyribonuclease recovery (9-10). In the pathophysiology of weakness in CKD, the most important pathway leading to muscle wasting is the adenosine triphosphate-dependent ubiquitin-proteasome system, which is stimulated by overexpression of myostatin and reduced satellite cell function (11).

Insulin resistance in patients with CKD is associated with the development of uremic myopathy, and in patients with diabetes mellitus on renal replacement therapy, it is even more severe (12). In patients with end-stage renal disease, type 2 diabetes mellitus can activate caspase-3 and the ubiquitin-proteasome system, thereby increasing muscle protein degradation. In addition, insulin resistance, by disrupting the insulin/IGF-1 signaling pathway in muscle, decreases phosphatidylinositol kinase and protein kinase Akt, an excess of angiotensin II, and proinflammatory cytokines. Uremic toxins and metabolic acidosis activate intracellular signaling pathways, leading to myofibril degradation. Two of the pathways leading to sarcopenia include activation of caspase-3, which destroys the complex structure of muscle protein, and low activity of protein kinase Akt, which reduces the phosphorylation of a transcription factor, thereby allowing it to be transported to the cell nucleus, where it stimulates the expression of factors that lead to muscle fiber atrophy. Patients have persistent inflammation, characterized by increased concentration of pro-inflammatory cytokines (C-reactive protein, interleukin-1, interleukin-6, tumor necrosis factor-alpha). Vitamin D deficiency plays an important role in the pathophysiology of sarcopenia and frailty. Vitamin D concentration is associated with muscle strength and physical performance. It plays an important role in the regulation of immunity, inflammation, insulin resistance, hypertension, cell proliferation, and differentiation, including the muscular system (13,14).

Thus, pathophysiological changes begin at the molecular level with damage to mitochondrial deoxyribonucleic acid (DNA), telomere shortening, oxidative stress, and inflammatory processes. The action of even a minor factor can trigger a cascade of adverse health reactions that can lead to fatal consequences.

Clinical picture of the frailty syndrome in chronic kidney disease

The diagnosis of chronic kidney disease is made in the presence of nephron damage and a reduced glomerular filtration rate (glomerular filtration rate (GFR)<60 ml/min) for 180 days. According to the glomerular filtration rate, CKD is divided into 5 stages (Table 1).

Table 1. CKD classification

Name	Stage	GFR value
CKD with normal DFR	1	>90 mL/m
Early CKD	2	60-89 mL/m
Mid-term CKD	3	30-59 mL/m
Severe CDK	4	15-29 mL/m
Terminal CKD	5	<15 mL/m or dialysis therapy

Source: compiled by the author.

In CKD, patients have the following symptoms: changes in urinary frequency and urine characteristics (frequent urination at night, pain and discomfort during urination, foamy urine, indicating a high level of proteinuria); peripheral edema (cold, more pronounced in the morning), itchy skin (due to the accumulation of uremic toxins in the blood); shortness of breath (as a result of iron deficiency anemia and/or fluid accumulation in the lungs); weakness and dizziness (due to reduced oxygen supply to the body); deficiency of active vitamin D and bone metabolism disorders (due to abnormal secretion of parathyroid hormone). In the terminal stages of CKD, severe respiratory system disorders (acidosis, pleurisy, pulmonary edema); digestive system disorders (uremic breathing, nausea, and vomiting, paralytic intestinal obstruction, acute pancreatitis) develop; Cardiovascular system disorders (heart failure, arrhythmia, uremic pericarditis); neuromuscular system disorders (headache, memory impairment, irritability, convulsions, cerebral edema, muscle weakness).

At stages 3-5 of CKD, frailty syndrome often develops. It is characterized by severe fatigue, weakness, weight loss, muscle weakness, impaired self-care, and cognitive dysfunction. The course of the disease is divided into 3 stages depending on the severity. The first is called the early stage (characterized by the onset of symptoms that do not significantly affect the quality of life). At the next stage, the symptoms limit the individual's normal functioning. A poor prognosis and a high risk of mortality characterize the third (or late) stage. A characteristic feature of the frailty syndrome in CKD is that it can develop in young patients, significantly worsening their quality of life and prognosis and increasing the risk of premature disability and mortality. Studies indicate that the prevalence of frailty syndrome among young patients on dialysis treatment is 35 % (15). In addition, 40 % of patients with CKD were diagnosed with pre-frailty (a transitional stage from a normal clinical condition to frailty) (16).

Diagnostic criteria for frailty syndrome in patients with CKD

Today, two diagnostic methods are relevant. These are the Frailty Scale and the Clinical Frailty Scale (17). The first method of assessment includes the following indicators: unintentional weight loss, subjective feelings of fatigue and exhaustion, a sense of weakness and reduced physical activity, slow walking speed, and reduced muscle strength in the arms. Weight loss is diagnosed by measuring the patient's body weight (a positive result is a loss of more than 5 kg in 12 months). The level of fatigue is assessed using the Centre for Epidemiologic Studies Depression Scale (CES-D) (18). Physical activity level is determined using the short version of the Minnesota Leisure Time Activity Questionnaire (19). Walking speed is assessed using the Stand and Walk test (which includes a 3 m round trip time, which should be more than 12 seconds to confirm the diagnosis) (20). Muscle strength of the arms is determined using a dynamometer, considering the patient's age and gender. The Fried's scale scores range from 0 to 5 points (one point for each of the above items). The presence of one or two of the above factors indicates an increased likelihood of developing

frailty in the future (pre-frailty state). Frailty syndrome is diagnosed with a score of 3 out of 5.

The Clinical Frailty Scale is a frailty assessment tool that considers specific areas of life, including comorbidities, independence, mobility, balance, the need for walking aids, and cognitive function. The criteria range from 1 (completely healthy) to 9 (terminal stage of the disease, life expectancy less than 6 months) points. The first 3 categories generally assess the patient's mobility, functioning, and thinking. The third to seventh category assesses mobility, self-care, and dependence on outside help. The eighth to ninth category is assigned to terminal stages of incurable diseases. A higher score means a higher risk of frailty.

Treatment of frailty syndrome in patients with CKD

Skeletal muscle atrophy begins in the early stages of CKD and progresses with the progression of renal failure. An imbalance between protein synthesis and breakdown causes atrophy. To effectively treat frailty syndrome, patients should be prescribed adequate nutrition: ensure sufficient protein, amino acids, and calorie intake. Add vitamin D, which increases bone strength and helps reduce the risk of falls and fractures. Also, it is worth increasing the daily calorie intake to 35 kcal/kg/day for patients undergoing dialysis treatment. Increase protein intake to 1.2 g/kg/day.

Sometimes, exercise, an appropriate diet, correction of metabolic acidosis, and treatment of comorbidities may not improve muscle function and mass. In such cases, hormone therapy is indicated: testosterone or growth hormone. This inhibits the accelerated loss of muscle fibers in patients with CKD (21-24). Neutralization of proinflammatory cytokines with gene therapy or anti-cytokine drugs suppresses muscle atrophy. Chronic kidney disease causes a decrease in the level of iron in the blood and the development of iron deficiency anemia (25). Therefore, it is necessary to monitor the complete blood count and, if required, prescribe recombinant human erythropoietin. After taking this medicine, patients experience an improvement in performance, strength, endurance, and quality of life.

Maintaining good psychological health reduces the risk of frailty. However, depression is common in patients with CKD, especially those on dialysis therapy. These individuals must adapt their current lives to the dialysis program. In addition, comorbidities and the use of many medications often lead to a deterioration in mental health, so it is important to use the Geriatric Depression Scale when selecting such patients and referring them to specialists for psychotherapy and/or antidepressants. Strong family ties, communication with like-minded people, and walks in landscaped areas can improve the overall psychological state (26-27).

Rehabilitation and prevention of frailty syndrome

Referral to rehabilitation therapy and mobilization of patients to exercise is the most important goal, as regular rehabilitation exercises prolong the period of independence of patients, reduce the risk of falls and fractures, positively change the course of chronic diseases, relieve pain, improve balance, increase bone strength, improve mental performance, reduce the number of medications taken, increase anabolism, and reduce pro-inflammatory cytokines. The quality of nutrition affects the risk of developing frailty syndrome. Foods directly and indirectly affect the inflammatory process and oxidative stress, which are components of the etiology of frailty syndrome. A healthy diet has been associated with a 10 % reduction in the risk of developing frailty syndrome (28,29).

Ni Lochlainn and Robinson (30) and Wu et al. (31) described the benefits of the Mediterranean diet. It consists of a high content of fruits, vegetables, nuts, seafood, and olive oil. Preference is given to the consumption of fish and seafood and a reduction in meat consumption. Fruits and vegetables contain polyphenols, which have anti-inflammatory and antioxidant effects. People who did not have frailty syndrome and ate 5-7 portions of fruit and vegetables daily had a lower risk of developing this pathology. This is due to fruits and vegetables' antioxidant properties and ability to suppress oxidative stress, reduce the production of reactive oxygen species, and protect DNA from damage. Omega-3 fatty acids contained in seafood also have anti-inflammatory effects. Thus, eating healthy foods

and exercising are important factors in treating, preventing, and rehabilitating frailty syndrome. The theoretical study presented here describes the features of frailty syndrome among patients with chronic kidney disease. At the same time, this syndrome often develops in the elderly, patients with type 2 diabetes mellitus, and patients with cardiovascular disease and rheumatological diseases.

Bąk et al. (6) found that 43 % of patients with frailty syndrome and diabetes mellitus 2 had symptoms of depression. Frailty syndrome is a risk factor for cognitive impairment, disability, and mortality among older people. Salis et al. (32) describe the main therapeutic areas in the combination of frailty syndrome and type 2 diabetes. They include the use of aerobic exercises and strength training. Physical activity positively affects the neuromuscular system, normalizes glycaemic levels, and reduces cardiovascular risk (33). The paper also describes that regular exercise increases protein anabolism, increases bone strength, and reduces pro-inflammatory cytokines. Salis et al. (32) noted that vitamin D intake helps to increase muscle strength, mass, and endurance. Similar results were obtained in the present study. Bąk et al. (34) determined that the frailty syndrome did not significantly impact the quality of life in patients with rheumatoid arthritis (RA). At the same time, Salaffi et al. (35) found that the prevalence of frailty syndrome among patients with RA and osteoarthritis (OA) was higher than in the general sample of geriatric patients. Pre-frailty syndrome is more common in cohorts of patients with RA than in cohorts of elderly patients (70 % and 55 %, respectively). With an overall prevalence of OA in any location of about 31 %, frailty syndrome was diagnosed in 10 % of patients and pre-frailty in 51 %.

Sławuta et al. (36) conducted a retrospective study of the impact of frailty syndrome on the quality of life in patients with atrial fibrillation. The study demonstrated that people with frailty syndrome had more severe arrhythmia symptoms and a lower quality of life. The prevalence of frailty syndrome among people with heart failure ranged from 20 % to 50 %. Common pathophysiological features explain the development of frailty syndrome against the background of cardiovascular disease. Chronic heart failure is associated with a change in the type of intermuscular fibers and reduced capillary wall density, which leads to mitochondrial dysfunction in skeletal muscle. Systemic inflammation develops adipose tissue increases, leading to decreased physical activity and the progression of the frailty syndrome. Hemodynamic disorders lead to tissue hypoxia, cellular apoptosis, and inflammation (37). Patients are at high risk of dyspnoea, poor sleep quality, and frequent depressive disorders.

Ma et al. (38) demonstrated that there is a causal relationship between bronchial asthma and frailty syndrome. The prevalence of bronchial asthma is about 300 million cases, and this pathology causes 250 000 deaths per year. Kusunose et al. (39) conducted a study and found that 75 % of elderly people with asthma had frailty syndrome. This is due to the presence of systemic chronic inflammation in patients with asthma. Inflammation causes an increase in eosinophils and total immunoglobulin E levels and increases catabolism. Given the advanced age and natural decline in immunity, asthma is a cause of frailty in the elderly. Figueiredo et al. (40) reported that frailty syndrome is a critical prognostic factor in patients with chronic respiratory diseases. People with chronic obstructive pulmonary disease and frailty had higher risks of hospitalization and falls and lower adherence to pulmonary rehabilitation.

Hoshino (41) found that the level of physical activity among patients on dialysis treatment is significantly lower than in the general population. This is due to the lack of mobility during dialysis itself and the presence of post-dialysis syndrome, which causes fatigue, nausea, and weakness. Dialysis also results in loss of muscle mass and strength, sarcopenia, mitochondrial dysfunction, osteoporosis, anemia, neurological disorders, and loss of 7-14 g of amino acids and albumin (42). The study also reported that dialysis therapy increases the risk of depressive disorders. These disorders lead to a low tolerance of patients with chronic kidney disease to physical interventions. For instance, Nitta et al. (43) indicated that about 80 % of Japanese elderly patients with a duration of dialysis treatment of more than 40 years were not used to exercise.

Polypharmacy (or taking many medications: 5 or more) is associated with adverse health outcomes, including increased risks of falls,

adverse drug reactions, more extended hospital stays, hospital-acquired infections, and death. Polypharmacy is also a risk factor for frailty. Gutiérrez-Valencia et al. (44) and Saum et al. (45) reported that the likelihood of frailty syndrome increases with each drug taken. This refers to physical weakness and the deterioration of psychological and social aspects of life. Cullinan et al. (46) reported that patients with frailty have twice the risk of adverse reactions than the general population. Athuraliya and Etherton-Beer (47) and Guo et al. (48) noted that the most common types of adverse reactions were cardiovascular pathologies, bleeding, and renal pathologies. This is especially true for elderly people who, due to several chronic diseases, are forced to take many medications constantly.

Zulfiqar et al. (49), Stamou et al. (50) and Lee et al. (51) noted that frailty syndrome significantly increases the risk of falling. The risk of falling increases with age and is 3.5 times higher in patients with frailty syndrome. Falls lead to injuries, hospitalization, several examinations, and a decrease in physical and social activity. In the elderly, the fear of falling and getting injured causes a slower gait speed and reduced mobility. About 47 % of elderly patients cannot get up on them after falling, even if the fall did not result in serious injury. Therefore, modern rehabilitation techniques are being actively developed to improve the functioning of patients with frailty syndrome. For example, Cicek et al. (52) and Lim et al. (53) reported that the use of Nintendo Wii technology (virtual reality technology, a commercial gaming device that uses a handheld game controller and a power platform) improved the individual physical performance of the study participants, reduced symptoms of depression, anxiety, and apathy, and improved memory and concentration.

The undeniable advantage of virtual reality and telerehabilitation technologies is the opportunity to work comfortably from home. Patients with frailty syndrome, regardless of age, have difficulty traveling to medical facilities, which can result in missing scheduled workouts. This technique is also relevant for people who, due to certain pathologies, feel more comfortable and safe staying at home rather than interacting with outsiders. The patients themselves positively evaluated virtual reality technologies after the study. In objective observations, virtual reality exercises helped improve older patients' motor and cognitive functions (53-55). The present study describes the benefits of physical therapy, and combining these two techniques can achieve better results in the rehabilitation and prevention of frailty syndrome.

The findings of this study have significant practical implications for both healthcare professionals and patients dealing with CKD and frailty syndrome. For healthcare professionals, the high frequency of frailty syndrome in patients with CKD emphasizes the importance of early detection and routine screening. Practitioners should be aware that 35 % of young dialysis patients experience frailty, indicating that it might impact even younger patients with CKD. This emphasizes the significance of thorough evaluations, utilizing instruments such as the Clinical Frailty Scale or Fried's Weakness Scale, regardless of the patient's age. Multimodal treatment plans should be used, with an emphasis on comorbidities, exercise, and diet. Patients may take greater responsibility for their care if they are aware of the connection between frailty and CKD. It is possible to control symptoms and enhance quality of life by exercising regularly, eating a balanced diet high in protein and other necessary nutrients, and actively participating in rehabilitation programs. The potential advantages of virtual reality and telerehabilitation technology provide new, easily accessible options for at-home treatment. These options may benefit patients with mobility challenges or who live in remote places.

CONCLUSIONS

Due to the increase in life expectancy and the rising incidence of chronic kidney disease, frailty syndrome is an important issue not only for geriatricians but also for nephrologists. Today, frailty syndrome is diagnosed in 60 % of patients with chronic kidney disease (mainly those with CKD stages 3-5). Frailty syndrome, which occurs against the background of the progression of chronic kidney disease, is characterized by changes in metabolism and

normal nephron function, the development of chronic inflammation, increased protein catabolism, metabolic acidosis, the accumulation of uremic toxins, and disorders of the endocrine and nervous systems. Hemodialysis used to treat CKD slows down protein synthesis, which decreases muscle mass and strength, exhaustion, fatigue, and weakness.

Frailty associated with CKD increases the risk of hospitalization and mortality. A high risk of developing frailty syndrome has been described in young people with a history of kidney disease. It is important to remember this for the early detection of this symptom and the prevention of complications. The main symptoms of the pathology mentioned above are unintentional weight loss, subjective feelings of fatigue and exhaustion, feelings of weakness and reduced physical activity, slow walking speed, and decreased muscle strength. The following diagnostic methods are currently effective: Fried's and Clinical Weakness Scales. The treatment, prevention, and rehabilitation of frailty syndrome is based on a healthy diet with all the necessary macronutrients, trace elements, and vitamins. Exercise is important because it prolongs the patient's period of independence, reduces the risk of falls and fractures, helps reduce pain and relieve pain, improves balance, increases bone strength, improves mental performance, helps reduce stress, increases anabolism, and reduces pro-inflammatory cytokines.

It is important to acknowledge several drawbacks of this study. Initially, the methodology is based on pre-existing research and could be influenced by bias in publication or constraints in the initial investigations. Furthermore, the research may have missed pertinent studies in other languages because it mainly concentrated on English-language sources. The extensive range of frailty syndrome examinations in connection to chronic renal disease and various age groups may have hindered a more detailed examination of particular subgroups or features of the illness. Moreover, a quantitative meta-analysis, which may have produced more accurate estimates of prevalence or effect sizes, was not carried out in this investigation. This study's limitations should be considered when interpreting and utilizing the results.

Based on these limitations, large-scale prospective cohort studies that monitor patients for an extended amount of time should be the focus of future research to gain a deeper understanding of the course and long-term consequences of frailty in this population. With respect to various subgroups, quantitative meta-analyses may yield more accurate estimates of prevalence and risk factors. Research should also look into how well different interventions work to prevent or lessen frailty in individuals with CKD. Furthermore, studies on the possible advantages of cutting-edge technologies for managing frailty in patients with chronic kidney disease (CKD), such as virtual reality and telerehabilitation, may provide insightful information. These initiatives would advance the understanding of frailty in CKD and help develop evidence-based management and preventive plans.

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