Assessment of nutritional status and nutritional habits in patients on hemodialysis

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ASSESSMENT OF NUTRITIONAL STATUS AND NUTRITIONAL HABITS IN PATIENTS ON HEMODIALYSIS

Diploma Thesis

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LIST OF ABBREVIATIONS

ACE - Angiotensin-Converting Enzyme

AKI - Acute Kidney Injury

AV - Arteriovenous

CKD - Chronic Kidney Disease

CVD - Cardiovascular Disease

DKD - Diabetic Kidney Disease

DMS - Dialysis Malnutrition Score

DNT - Dietetic Nutritional Therapy

ECFV - Extracellular Fluid Volume

eGFR - Estimated Glomerular Filtration Rate

ESRD - End-Stage Renal Disease

HD - Hemodialysis

KDIGO - Kidney Disease: Improving Global Outcomes

MDSS - Mediterranean Dietary Serving Score

MIS - Malnutrition Inflammation Score

NSAIDs - Nonsteroidal Anti-Inflammatory Drugs

PTH - Parathyroid Hormone

RAAS - Renin-Angiotensin-Aldosterone System

ROS - Reactive Oxygen Species

1. INTRODUCTION

1.1 Chronic kidney disease

1.1.1 Definition

Chronic kidney disease (CKD) has been defined by the Kidney Disease: Improving Global Outcomes (KDIGO) international guidelines as an abnormality of kidney structure or functioning being present for more than 3 months impacting on health (1).

This decrease in kidney function is defined as a permanent reduction in the estimated glomerular filtration rate (eGFR) to less than 60 mL/min/1.73 m^2 or 1 or more markers of kidney injury such as albuminuria or an abnormal urine sediment (1). Additionally, it is important to mention that CKD is a progressive disease which can lead to end-stage renal disease (ESRD) as its final result leading to major morbidity and mortality and furthermore tremendous financial health care expenses (1,2). ESRD ultimately can lead to chronic renal failure (CRF) which is a condition marked by an eGFR of <15mL/min/1.73m^2 (3). This condition requires long-term therapy with hemodialysis (HD) and possibly renal transplantation (3).

1.1.2. Epidemiology

CKD has an overall prevalence of 10-15% in the global adult population and it further increases (4). The disease may slightly more commonly affect women than men, but there is no significant difference in prevalence between the genders (5). Additionally, it is worth mentioning that the prevalence of CKD is increasing with age (5). Generally, the prevalence of CKD is higher in high income industrialized countries compared to low income developing countries (5). In the United States there was an increase in the prevalence of CKD from the 1990s to the early 2000s, however the prevalence stabilized in the 2000s and is now on a relatively stable level (6). In Iran, which still is a developing country, the prevalence of CKD is similarly high like in the developed world, which may be due to a comparably high prevalence of common CKD risk factors (5).

In numbers, the prevalence of CKD in the industrialized world, for example Europe, is around 18.4%, in the USA and Canada it is slightly lower with only 15.5% (5). In Australia, the prevalence of CKD is around 14.7 % (5). In developing countries, such South Africa, Senegal and Congo the CKD prevalence is about 8.7%, so it is lower than in highly developed

countries (5). In many Asian countries, such as India and Bangladesh the prevalence of CKD is 13.1% or slightly above (5).

1.1.3 Risk factors

Risk factors for CKD can be divided into factors that lead to initial development of the disease and furthermore factors that lead to chronic disease progression (7). Well known initiating factors for CKD are hypertension, diabetes mellitus, male sex, advanced age and African-American ethnicity (7,8). Furthermore, chronic renal disease can be caused by several inheritable intrinsic renal diseases that can also be transmitted over several generations in families, like autosomal-dominant polycystic kidney disease and the Alport´s syndrome and even inborn errors of metabolism like Fabry´s disease (8). Another important condition that markedly increases the risk for CKD and even ESRD is acute kidney injury (AKI) which might regress after the underlying condition resolved but can also permanently damage to kidney to the degree of CKD (9). Evidence has also shown that obesity and the metabolic syndrome can lead to the development of CKD (8). Other less well-known initiating factors of chronic renal disease are dyslipidemia and hemoglobinopathies (8).

It is important to notice that most of these initiating factors can also participate in disease progression to CRF and consequently ESRD (7,8). Especially risk factors for cardiovascular disease (CVD) such as hypertension contribute to CKD progression and CKD also exacerbates CVD risk factors leading to a vicious cycle (8,10). Additionally, increasing age is a major factor associated with an increased incidence of ESRD and thus CKD progression (8). Men show a higher incidence of proteinuria and thus have a higher risk of CKD progression, as proteinuria and hyperfiltration states facilitate nephron loss and consequently kidney injury (7,8). Profound proteinuria additionally leads to decreased serum albumin levels which is a good serum marker for progressive renal disease (8). It is worth noticing that certain lifestyle factors, such as smoking also increase the risk of CKD progression by facilitating diabetic or hypertensive nephropathy, whereas alcohol consumption is not clearly associated with a risk of CKD (8,10). Another important factor and also a marker for progressive chronic renal disease is hyperuricemia (8,11). Hyperuricemia can lead to CKD progression because it causes an increase in glomerular filtration pressure, endothelial dysfunction and it further exhibits proinflammatory effects (8). Hyperuricemia is influenceable by lifestyle interventions that can decrease the risk for CKD and its progression (12). These factors include regular exercise,

weight loss, a restriction of purine-rich meat and avoiding a diet high in fructose which can also modify other CKD risk factors like CVD (12,13).

1.1.4. Pathophysiology

CKD is marked by kidney injury leading to a permanent decrease in eGFR to less than 60mL/min/1.73m^2 or 1 or more markers of kidney disease like albuminuria or an abnormal urine sediment (1). The chronic kidney injury can be precipitated by many different factors like hypertension and diabetes which are common causes of CKD (7,8).

Hypertension is one of the major CVD risk factors that is strongly related with the development of CKD (14-16). The pathophysiology of hypertension and CKD are closely intertwined, leading to a complex relationship between these 2 disease entities (10,14-16). Around 60-90% of patients with CKD suffer from hypertension, which is an initiating risk factor of the disease that causes profound glomerular damage by glomerular hypertension and nephrosclerosis and precipitates loss of kidney function over time (8,10,14). Hypertension is also a consequence of CKD and an exacerbating factor that leads to long-term deterioration in CKD (8,10,14). The mechanisms of development and exacerbation of hypertension in CKD patients include sodium retention from loss of nephrons and glomerular filtration which leads to volume overload (14). Furthermore, patients with CKD frequently present with sympathetic overactivity which leads to further sodium retention and peripheral vasoconstriction (14,16). Other pathophysiologic factors that worsen hypertension and can cause glomerular injury are endothelial dysfunction and hormonal dysregulation of the renin-angiotensin-aldosterone system (RAAS) (14,16). Ultimately, a chronically elevated blood pressure can cause progression to ESRD (15).

Diabetic kidney disease (DKD) is a major cause of CKD and thus plays a crucial role in the pathophysiology of CKD (7,8,17). DKD is a microvascular disorder caused by an elevated plasma glucose facilitating endothelial injury in diabetic patients leading to progressive kidney dysfunction and development and progression of CKD (17). Hyperglycemia causes generation of reactive oxygen species (ROS) which causes DNA injury to endothelial cells and leads to cellular dysfunction, inflammation, fibrosis and apoptosis in cells exposed to the elevated plasma glucose level causing glomerular injury (17). DKD is a multifactorial entity displaying a complex pathogenesis which includes metabolic factors, like elevated fatty acids, oxidative stress, and furthermore hemodynamic factors that cause shear stresses to the glomeruli and renal vasculature, such as systemic hypertension, dysfunctional autoregulation of the renal vascular

beds, hypoperfusion or hyperperfusion of the kidney and an abnormal RAAS activation (17). Diabetic changes in the glomerulus are progressive (17). Early in the disease the podocytes become dysfunctional and the glomerular basement membrane thickens inside the glomerular capillary tufts (17,18). This podocytopathy seen in CKD is a strong predictor of renal disease progression (17,18). Additionally, DKD is marked by recruitment of inflammatory cells which migrate into the glomerulus and damage the filtration barrier of the glomerular capillary tufts (7,8,17). This leads to hyperfiltration and progressive albuminuria that can further exacerbate the nephropathy (7,8,17). It is worth noticing that DKD not only causes a glomerulopathy but it can even cause loss of renal tubules by tubulointerstitial fibrosis which is seen in a high percentage of glomeruli in patients with DKD (17).

CKD is also commonly aggravated by existing proteinuria, which resulted from previous kidney injury and led to chronic renal disease and even ESRD (19,20). Proteinuria is caused by alterations in the structure or function of the glomerular filtration barrier or by defects in the renal tubules (19). Especially in nephrotic syndrome, proteinuria is a hallmark of disease and can cause interstitial inflammation and fibrosis and it also can induce apoptosis and impaired autophagy of proximal renal tubular cells (19). Specifically, albuminuria can injure renal tubular tight junctions and cause inflammation and fibrosis in the renal cortical collecting ducts (19). Long-standing proteinuria is a strong predictor of CKD progression to ESRD (19). It is important to know that treating and thus decreasing proteinuria can slow down progression of the pathophysiologic cascade that ultimately results in ESRD (20).

The reduced renal ability to maintain the body´s fluid and electrolyte homeostasis in CKD leads to derangement of multiple parameters like an altered serum potassium level, bone mineral disorders and also metabolic acidosis (21). Hyperkalemia is a leading cause of life-threatening electrolyte disorders in advanced CKD and ESRD and it is mainly caused by an impaired renal potassium excretion ability (21). Hypokalemia however is a rare derangement sometimes found in CKD patients and is mainly caused by persistent vomiting or diarrhea (21). Patients with CKD also have a decreased ability to reabsorb bicarbonate and a decreased capacity of acid excretion (21,22). This leads to the development of metabolic acidosis in such patients (21,22). It is important to know that patients with advanced renal disease suffer from vitamin D deficiency because they cannot metabolize and thus convert this hormone into its active form (21,23). This leads to a compensatory secondary hyperparathyroidism that in turn causes hypercalcemia and hyperphosphatemia which cannot be compensated by the impaired kidneys leading to vascular calcification which additionally disables kidney function and bone

mineral disorders (21,23). Additionally, hyponatremia can occur due to decreased urine concentrating ability of the kidney and hypermagnesemia can occur as a consequence of markedly reduced eGFR (21).

1.1.5. Clinical picture

The clinical manifestations of CKD include a broad spectrum of disorders, e.g. fluid and electrolyte disorders, acid-base derangements, endocrine and skeletal disorders, uremic syndrome which includes uremic pericarditis and neurologic disorders, CVD, gastrointestinal and nutritional abnormalities, dermatologic abnormalities and hematologic abnormalities such as anemia and hemostatic disorders (24).

In patients with CKD the amount of sodium and water excretion and intake is mismatched since eGFR is decreased and the resulting salt and water retention can frequently cause edema, especially in advanced disease (24,25). The salt and water retention leads to an isotonic increase in extracellular fluid volume (ECFV) which can cause hypertension (24,25). The increase in ECFV also precipitates peripheral and pulmonary edema commonly seen in CKD patients (24,25). Another cause of edema is albuminuria which is found in nephrotic syndrome (24,25). A major electrolyte disturbance that is often encountered in CKD patients and can have serious sequelae is hyperkalemia, which can have many different reasons ranging from too high potassium intake and decreased potassium excretion to drugs that inhibit the RAAS (21,24). Hypokalemia is a less common entity in those patients however it can occur in states of gastrointestinal losses of potassium or extensive diuretic therapy (21,24).

The acid-base derangement most commonly found in CKD is metabolic acidosis, especially in advanced disease (24). This acid-base disorder frequently presents with protein catabolism that presents clinically with muscle wasting, endocrine disturbances and an increased mortality (21). Generally, in earlier stages of CKD a non-anion-gap metabolic acidosis is seen, which can be worsened to an anion-gap metabolic acidosis as ESRD appears (24).

The main endocrine disturbances encountered in CKD patients are secondary hyperparathyroidism, which means an elevated serum parathyroid hormone (PTH) level due to hyperplasia of the parathyroid glands, and $1,25(OH)_2D_3$ or calcitriol deficiency leading to severe disturbances of the calcium and phosphate metabolism (21,24,26). The decreased production of calcitriol by the chronically failing kidney leads to a decreased serum calcium

content which in turn causes the secondary hyperparathyroidism that ultimately will present clinically with hypercalcemia and hyperphosphatemia (21,24). The chronically elevated PTH level over time will result in skeletal disorders such as renal osteodystrophy and osteoporosis in CKD patients (21,24,26). The decreased bone mineral density (BMD) seen in renal osteoporosis clinically presents with an increased frequency of fractures (26). Furthermore, long-standing hyperparathyroidism with hyperphosphatemia can clinically present with osteitis fibrosa cystica and can also lead to tumoral calcinosis after many years (21,24).

Uremic syndrome is a clinical entity encountered in patients with progressive renal failure which can have multiple deleterious effects including neurotoxicity of uremic toxins, metabolic and electrolyte derangements, secondary hyperparathyroidism, anemia, thiamine and vitamin D deficiency, hyperhomocysteinemia and coagulation disorders (24,27). Neurologic effects of uremia include cranial neuropathy, especially of the acoustic and olfactory nerves and uremic myopathy which includes proximal muscle weakness with atrophy of muscle fibers (28). Additionally, peripheral neuropathy with muscle weakness might be seen (24,28). A very severe clinical presentation of uremic syndrome is uremic pericarditis which might even present with pericardial effusion (24,29). Pericarditis in light of severe uremia is defined as an emergency situation in CKD patients which requires prompt therapy (24,29). Uremic toxin accumulation can also lead to anorexia, nausea and vomiting (24).

Cardiovascular disease is closely related to CKD as hypertension is a common feature of CKD and also an exacerbating factor of the disease (10,24). Long-standing hypertension can precipitate left ventricular hypertrophy that may ultimately present with heart failure (24,30). Left ventricular hypertrophy leads to heart failure with diastolic dysfunction (24). The resulting volume and pressure overload on the heart presents with congestive heart failure symptoms such as peripheral and pulmonary edema (24). Atrial fibrillation can occur as a consequence of the underlying structural cardiac changes (24,30). In addition, ischemic vascular diseases can result from long-standing hypertension and CVD in CKD patients, namely coronary artery disease, cerebrovascular disease and peripheral vascular disease (24,30). Another more specific vascular disease entity is vascular calcification which presents as deposition of calcium phosphate salts into blood vessels which leads to increased morbidity from vascular disease (24,31).

Patients with advanced CKD and ESRD often present with gastrointestinal and nutritional abnormalities (24,32). Those patients usually have to take in many different medications, such as diuretics, iron supplements and oral phosphate binders, which can slow

bowel motility and lead to chronic constipation (32). Additionally, these patients face many dietary restrictions which often adversely affects intestinal peristalsis by being on a diet that is usually also low in fiber (32). One of the most important nutritional abnormalities is the so-called protein-energy malnutrition which is commonly described to be consequence of low protein and caloric intake (24,32). The existing metabolic acidosis further exacerbates protein catabolism and thus contributes to muscle wasting from the nutritional protein deficiency (24,32).

Cutaneous manifestations are frequently seen as symptoms of advanced CKD (24,33). Uremia commonly causes pruritus in CKD patients (24,33). Very commonly seen in this patient population are xerosis, pallor, itchiness, cutaneous pigmentation and dermatitis (33). A very specific condition confined to CKD patients is nephrogenic fibrosing dermopathy which generally presents with progressive subcutaneous induration found on the extremities and is specifically seen in patients exposed to the MRI contrast agent gadolinium (24).

The hematologic manifestations of CKD play an important role the clinical picture of the disease and a major condition affecting these patients is anemia (24,34). The anemia presents with fatigue, dyspnea, decreased physical fitness, loss of appetite, impaired immunity and neurocognitive dysfunction (34). The most important factor that leads to the normocytic, normochromic anemia is a reduced production of erythropoietin which is thought to be the main etiology of renal anemia (24,34). Additionally, CKD can also cause anemia of chronic disease, which is due to decreased absorption of iron from the gut and inhibited utilization and trapping of iron in the body because of hepcidin overproduction (34). The anemia in advanced CKD can further provoke progressive heart failure and impaired oxygen delivery to tissues (24). Another frequently encountered hematologic problem is an abnormal hemostasis that can occur in patients with advanced CKD (24). Patients with advanced CKD present with a bleeding diathesis with longer bleeding time, abnormal platelet aggregation and adhesiveness and an impaired prothrombin consumption caused by uremic syndrome (24). This prolonged bleeding time may also be due to a poor vitamin K status that results from the restricted diet which CKD patients have to follow (35). However, patients with nephrotic range proteinuria lose so many antithrombotic factors that they in fact are at risk of venous thromboembolism because they are in a thrombophilic state (24).

1.1.6 Diagnosis

The diagnostic approach in CKD starts with evaluation of the patient´s medical history and physical examination (24). In the early stages of CKD patients are often asymptomatic or only have subtle symptoms which sometimes can lead to a delay in diagnosis (24,36). A careful family history should be established since kidney diseases often run in families (24). During history taking, patients should also be asked when possibly related conditions like hypertension, diabetes mellitus and proteinuria have started and whether there were previous check-ups where serum creatinine test have been performed (37). Furthermore, the patient should be asked if he noticed any symptoms of decreased kidney function like those related to uremic syndrome, urinary obstruction and fluid overload (24). Additionally, a precise drug history has to be established since many widely available drugs like nonsteroidal anti-inflammatory drugs (NSAIDs) can lead to renal failure (37). The physical examination mainly focuses on blood pressure, signs of fluid overload and detection of end-organ damage (24,37). Furthermore, if the patient has diabetes mellitus, possible end-organ changes in the eye should be checked for (37).

Next, laboratory tests, mainly blood count, blood chemistry and urinalysis should be performed (24,37). This includes complete blood count and measurement of serum creatinine as well as electrolytes and hormone levels, especially vitamin D and PTH (24). The diagnosis of CKD is nowadays mainly based on the finding of an elevated serum creatinine concentration which indicates a decreased eGFR but this marker is not sensitive in early stages of CKD (36,37). The other mainstay of laboratory diagnosis of CKD is urinalysis (36). This is an essential diagnostic measure because urine is a more stable sample than blood and it is an easy, fast and cheap method because there are many kinds of rapid urine dipstick tests possible that can detect proteinuria, albuminuria, hematuria, bacteriuria and pus in urine (36). It includes 24-hour urinary protein excretion measurement and several highly specialized measurements like urine protein electrophoresis that can detect different underlying etiologies of CKD (37).

An essential part of making and accurate CKD diagnosis is renal ultrasonography (37,38). It is a very popular diagnostic method for diagnosis and also monitoring of CKD since it can easily visualize kidney anatomy, renal blood flow, eGFR, differentiate between AKI and CKD which is important in initial diagnosis of kidney disease (24,38). This technique nowadays even uses contrast media to better visualize renal vasculature (38). Further imaging studies that have a role in CKD are nuclear medicine techniques, CT and MRI (24).

Ultimately, an invasive technique important for diagnosis of the underlying pathology is a kidney biopsy (24,39). It is known to be the gold standard of diagnosis of kidney diseases (39). Kidney biopsy samples are evaluated by microscopy and immunohistologic techniques to make a diagnosis (39). Precautions must be taken since there are numerous contraindications to renal biopsy like uncontrolled hypertension, urinary tract infection and bleeding diathesis (24).

After establishing the diagnosis of CKD, the disease can be classified using the Kidney Disease Improving Global Outcomes (KDIGO) classification of CKD, which takes into account the eGFR and degree of albuminuria (Figure 1). It is important for prediction of prognosis of CKD patients (1).

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30–300 mg/g 3–30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min per 1.73 m²) Description and range	G1	Normal or high	⩾90			
	G2	Mildly decreased	60–89			
	G3a	Mildly to moderately decreased	45–59			
	G3b	Moderately to severely decreased	30–44			
	G4	Severely decreased	15–29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red, very high risk.

Figure 1. A diagram presenting the KDIGO classification of CKD using glomerular filtration rate and albuminuria to determine the prognosis of CKD (1).

1.1.7. Treatment

Treatment of CKD mainly focuses on slowing down the progression of disease to ESRD (24). Slowing down of progression of CKD by preserving the eGFR with maintenance treatment will delay progression to ESRD and thus patients will have a longer time without the need for dialysis or renal transplantation (37).

One of the most important measures for preventing disease progression is a reduction of intraglomerular pressure and proteinuria to decrease the filtration pressure and trauma to the

glomerular tufts (24). This can be achieved by usage of antihypertensive medications, especially angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blockers which reduce intraglomerular pressure by dilating the efferent arteriole (24). This therapy also leads to a decrease in filtration pressure and proteinuria and treats arterial hypertension, a common comorbidity (24). Arterial hypertension should be decreased to a goal blood pressure of less than 140/90 mm Hg (15). Proteinuria can also be reduced by prescribing a diet low in salt and fat to decrease the risk of CVD which causes an increased mortality in CKD patients (37).

In addition, it is crucial to aggressively provide glycemic control in diabetic patients since diabetic nephropathy with glucosuria is a great risk factor for disease progression (7,37). Patients with nephrotic syndrome should not receive nephrotoxic drugs like NSAIDs, radiocontrast agents or gadolinium because these can further damage the glomeruli and acutely exacerbate the condition (24,37).

The fluid and sodium imbalance should be treated with salt restriction and loop diuretics which are first choice agents in treating ECFV expansion since most CKD patients are salt-sensitive (25). Sodium intake should measure less than 2g per day (25). This a positive impact on left ventricular hypertrophy which is associated with and increased ECFV (25).

Other comorbidities of CKD should also be treated, for example anemia which requires erythropoietin analog administration (34). Osteoporosis and renal osteodystrophy is usually treated with calcitriol supplementation and calcimimetics, but antiresorptive agents like bisphosphonates are frequently used (26). Hyperuricemia which causes disease progression in CKD is addressed with dietary and lifestyle changes or allopurinol in more severe cases (12). It is important to prevent hyperphosphatemia by dietary phosphate restriction and administration of oral phosphate binders (21).

Finally, patients have to become educated about their chronic disease and ultimately be prepared for renal replacement therapy by HD or peritoneal dialysis with the ultimate goal of a renal transplantation (24). The time to dialysis should be delayed as much as possible but ultimately dialysis should not be initiated too late for a better outcome in ESRD (24). Kidney transplantation offers the most efficient replacement of renal function, because dialysis only replaces a small part of a healthy kidney´s filtration function (24).

1.2 Hemodialysis

Criteria for starting maintenance HD in ESRD patients are the presence of uremic symptoms, hyperkalemia that cannot be corrected otherwise, ECFV expansion resistant to diuretic therapy, persistent metabolic acidosis, a bleeding diathesis and an eGFR of less than 10 mL/min per 1.73 m^2 (40).

Conventional HD using 3 sessions with 9-12 hours of weekly dialysis is nowadays sometimes replaced by specific regimens like long intermittent hemodialysis, short daily HD and daily home nocturnal HD (40,41). Long intermittent HD follows a regiment of 8 hours of dialysis for 3 times per week (41). This regimen allows for excellent blood pressure control however it does not influence on left ventricular hypertrophy (41). Short daily HD is performed for 2-2.5 hours per day on 6 to 7 days per week (41). It is better tolerated than conventional HD and allows for better solute removal (41). Furthermore, the erythropoietin dose required is decreased in this type of HD (41). Daily home nocturnal HD is performed during sleep for 8 hours in 6 or 7 nights per week (41). The dose of dialysis is higher than in conventional HD and removal of phosphate is markedly enhanced (41). Patients report a better quality of life and show regression of left ventricular hypertrophy and even sleep apnea (41). Generally, the goal of HD is an individualized approach to the patient with a dose of dialysis that promotes adequate fluid removal, correction of electrolyte abnormalities, uremia and metabolic acidosis with preservation of an adequate patient quality of life (40,41).

The physical principles of HD are based on solute diffusion across a semipermeable membrane down a concentration gradient from the patient´s circulation into the dialysate (40). Corresponding with the laws of diffusion larger molecules such as creatinine are cleared more slowly from the patient´s blood than smaller molecules like urea (40). Additionally, ultrafiltration across the dialysis membrane and convective clearance, which means that solutes are dragged across the membrane along with osmosis of water molecules (40).

HD machines use 3 main components, the dialyzer which is made up of specialized membranes, the dialysate which is required for solute exchange and the blood delivery system (40).

The dialyzer is a chamber than simultaneously contains the blood and the dialysate at high flow rates which are separated by a semipermeable membrane for solute exchange (40). Most commonly used are hollow-fiber devices which uses tubes through which the blood circulates and which are bathed in the dialysate (40). Nowadays, the membrane is a biocompatible synthetic membrane made of polysulfone or similar compounds, which is an

advance since the bioincompatible membranes that were used before activated the complement cascade (40). A new generation of membranes are medium cut-off (MCO) membranes (42). These have the ability of improved clearance of large molecular weight solutes while avoiding significant albumin loss (42).

The dialysate contains water, electrolytes and other compounds found in the patients serum, but at lower concentration to drag the accumulated solutes out of the patients serum (40) Special attention is given to potassium, sodium and calcium since these electrolyte can have markedly influenced serum levels after dialysis which can exhibit physiologic effects (40). The dialysate potassium level can range between 0-4 mmol/L (40). The physician has to carefully adjust the dialysate´s potassium level to not differ too extremely from the patient´s serum potassium concentration since this could lead to arrhythmias and increased cardiovascular mortality (43). It is worth noticing that the calcium concentration in the dialysate is also crucial in patients with dyscalcemias and can be increased in cases of hypocalcemia in secondary hyperparathyroidism and vice versa (40). The sodium level is mainly important for fluid balance (40). To prevent intradialytic hypotension the sodium content can be elevated however this might predispose to arterial hypertension (40).

Next, the blood delivery system consists of the extracorporeal circulation and the dialysis access (40). This system is run by a blood pump which draws the blood from the patient´s circulation via the dialysis access, through the dialyzer and back to the patient (40). The different types of HD vascular access include arteriovenous (AV) fistulas, AV grafts, and central venous catheters (44). The recommendation promotes AV fistulas to be used first since they have a better clinical outcome, a decreased risk of infection and thus fewer hospitalizations and lower mortality rates (44). AV grafts tend to require more interventions and are more likely to fail (44). Central venous catheters are the most commonly used method for dialysis initiation because of the ease of placement in patients but they are inferior to AV fistulas in mortality (44).

Possible adverse events of HD include hypotension, dialysis disequilibrium syndrome, air embolism, hemolysis, venous needle dislodgement, muscle cramps, allergic reactions and adverse reactions with intravenous iron (40,45). Hypotension is the most common acute adverse effect which can occur due to excessive ultrafiltration, osmolar shifts, reduced cardiac function and impaired autonomic responses (40). Shunt flow of blood through AV fistulas or AV grafts can over time lead to a high-output heart failure (40). Emergencies include those related to the dialysis water system and potentially fatal vascular access hemorrhage (45). Vascular access

hemorrhage most commonly occurs outside of the healthcare facility but it is a severe complication that requires prompt intervention and adequate patient education (45).

Ultimately, it is worth noticing that patients on HD generally report a poor quality of life (41). This poor quality of life is the result of symptoms of uremic syndrome, the burden of the HD procedure itself, and the presence or occurrence of comorbid conditions (41). Recently patient mortality has improved, but it is still very high with 15-25% of patients dying every year with CVD being the most common cause of death (41).

1.3 Nutrition in CKD patients

Nutrition is an important aspect in treatment and prognosis of CKD patients since controlled dietary intake of energy, protein, sodium and phosphorus are crucial for renal protection (46). An altered nutritional status in CKD patients can lead to various sequelae which include metabolic acidosis, intestinal dysbiosis and hormonal disturbances all of which can lead to renal disease progression and an increased morbidity and mortality (32). Patients are counselled and advised to stay on a specially restricted renal diet (47). This has led to an increasing importance of dietetic-nutritional therapy (DNT) which is a major part of the conservative treatment and maintenance of patients with CKD (47). It is worth noticing that DNT should be used in conjunction with other health interventions such as pharmacotherapy (47). DNT involves modulation of protein intake, an adequate caloric intake, control of sodium, potassium intake and also a restriction of phosphorus intake (47).

Of considerable concern in CKD is the fact that patients with chronic renal disease are commonly facing protein malnutrition since they are in a protein catabolic state (32). This so-called protein-energy wasting is defined as abnormally low levels or excessive losses of lean body protein and energy stores which is frequently observed in CKD patients, especially in patients undergoing HD (48). This occurs on the one hand because of inappropriate nutrient intake since patients with CKD often suffer from uremic syndrome which can cause decreased appetite, nausea and vomiting (24,48). On the other hand, it occurs due to persistent inflammation and oxidative stress, an altered glucose and insulin metabolism, metabolic acidosis, a catabolic state and vitamin D deficiency which can cause muscle wasting and protein loss (24,48). Protein-energy wasting and malnutrition in fact increase mortality in CKD patients (48). Patients with CKD are usually prescribed a low protein diet because this results in better control of uremic symptoms, decreased proteinuria and hyperfiltration and it reduces the patient´s sodium, phosphorus and inorganic acid level (49). This low protein diet is commonly

combined with increased intake of complex carbohydrates to counteract against the energy wasting and improve the patient´s nutritional state (50). Thus, protein restriction positively affects the disease outcome and also delay to time to ESRD requiring dialysis (46,49). In general, the lower renal function is, the more the restriction on protein intake increases for renoprotection (49). Sometimes, also a very low protein diet with supplemented ketoacids might be used in CKD stage 5 patients to delay the initiation of dialysis (49). This improves many parameters such as metabolic acidosis, hyperparathyroidism, hyperphosphatemia, dyslipidemia and uremia (49). It additionally has beneficial effects on blood pressure and proteinuria without affecting the nutritional status (49). In patients on HD however, an increase in dietary protein intake is required, as this has shown to lead to improved mortality and is therefore recommended by current guidelines (48).

The ingestion of complex carbohydrates and dietary fiber should be increased in CKD patients, since these provide a high caloric value needed to treat the catabolic state and has only a negligible content of nitrogen, potassium and phosphorus (50). This can be accomplished by intake of cereal grains or psyllium (50). Dietary fiber has benefits by restoring the gut microbiome, which progressively worsens as CKD progresses (50). By restoring the gut microbiome, there is fewer accumulation of uremic toxins thus decreasing systemic inflammation (50).

Fatty acids play an important role in nephrotic syndrome where serum lipid profiles are generally altered (49). These patients have decreased serum levels of omega-3 and increased levels of omega-6 fatty acids and other lipids (49). An association between this lipid imbalance and progression of renal disease has been reported (49). The role of omega-3 fatty acid supplementation in CKD patients, however remains controversial (49).

It is worth noticing that CKD patients commonly suffer from hyperphosphatemia (48). This electrolyte disturbance is primarily corrected through dietary phosphate restriction, the administration of oral phosphate binders and dialysis (48). To the benefit of CKD patients, their frequently prescribed low protein diet concomitantly leads to a decreased dietary phosphate intake (48). The phosphorus pyramid, designed by D´Alessandro et al. helps patients to stay compliant with a low phosphate diet, since it presents protein-restricted foods that are at the same time low in phosphate (48). Patients taking oral phosphate binders are known to demonstrate a better nutritional status and thus survival (48).

Another crucial nutritional measure is dietary sodium restriction, which is effective in lowering salt-sensitive hypertension and fluid retention that are often present in CKD patients

(48). High salt intake is also associated with direct renal damage and increased albuminuria and thus is to be prevented (48). Furthermore, also potassium intake needs to be carefully controlled which should be oriented towards the serum potassium levels and be decreased if hyperkalemia occurs (47). This is especially of consideration in cases of advances CKD (47).

Supplementation of vitamin D in CKD patients is frequently done, because CKD patients cannot activate this vitamin in their damaged kidneys to a sufficient extent (51). Lower serum calcitriol levels are associated with a worse cardiovascular outcome and thus should be supplemented in this patient population (51). Additionally, patients on hemodialysis are often deficient in water soluble vitamins such as vitamin C, folic acid and B vitamins which should therefore be supplemented in the diet (52). Iron deficiency is another major health issue that can lead to anemia in hemodialysis patients which is a common finding in these patients (52).

Finally, intradialytic feeding is a method to reduce catabolism during hemodialysis that can improve nutritional status in ESRD patients (53). It may be especially effective in the morning after an overnight fast since patients are already in a catabolic state after the night (53). The procedure has been shown to improve nutritional reserve, prealbumin and also serum albumin (53). Intradialytic feeding can benefit both, patients with protein-energy wasting and those without (53). Adverse effects of intradialytic feeding can be intradialytic hypotension in specific patient populations, such as diabetics (53).

2. OBJECTIVES

The aim of this study was to assess the nutritional status and adherence to the Mediterranean diet in patients on HD treatment.

Hypothesis:

1. Patients on HD will have low adherence to Mediterranean diet.
2. Patients on HD will have high MIS and DMS scores.
3. There will be negative correlation between MIS and DMS scores and body fat percentage in patients on HD treatment.
4. Women will have higher percentage of body fat, MIS and DMS scores in comparison with men on HD.

3. SUBJECTS AND METHODS

This study was performed in a period between September and November of 2018 at Department of Nephrology, University Hospital of Split. All included participants signed informed consent form and they were able to ask any questions about the study procedures before the start of the measuring.

3.1. Participants and methods

In this study, 55 patients on HD treatment at Department of Nephrology were enrolled. Patients had to be older than 18 years, and underwent HD at least for 6 months. Patients with any form of acute infection or malignancy were excluded from the study.

Detailed medical history with daily habits assessment and clinical examination were taken from each subject. Body height and weight (before and after HD treatment) were measured with calibrated scale. Waist and hip circumference were measured in upright position according to standard guidelines (54). Furthermore, venous blood samples were taken from all subjects, and assessment of lipid panel, total protein and albumin levels was made using standard biochemical procedures.

3.1.1. Mediterranean diet

After clinical assessment and venous sampling, all participants filled Mediterranean Diet Serving Score (MDSS) questionnaire (55). MDSS assessed dietary habits on basis of Mediterranean Diet Pyramid (56). Following the guidelines, if subjects fulfilled according frequency of different food groups consumption, points were given. Olive oil, cereals, fruit and vegetables were groups that were evaluated as 3 points; milk, dairy products and nuts 2 points; potatoes, eggs, fish, white meat, legumes, red meat, sweets and wine 1 point. If the subjects did not follow eating recommendations for individual food group, no points were given. Accordingly, highest number of points in MDSS questionnaire was 24, and score >13.5 was considered as good adherence to the Mediterranean diet guidelines.

3.1.2. Body fat calculation

During clinical examination, all participants underwent measuring for body fat percentage estimation. Standard caliper for measuring skin fold thickness was used for this purpose, using Jackson/Pollock 3 caliper method.

In male subjects, skin fold thickness at three body points was measured – chest point (diagonal fold, between armpit and nipple); abdominal point (vertical fold, an inch to the right of navel); and thigh point (vertical fold, between kneecap and top of thigh). In female subjects, thigh fold was the same, but other two areas were triceps point (vertical fold, between elbow and shoulder) and suprailiac point (diagonal fold above iliac crest).

Skin fold thickness in millimeters was inserted into available online calculator (57) for each of the subjects, and body fat estimation percentage was recorded.

3.1.3. Nutritional status

For the purpose of nutritional status assessment of HD patients, two standardized questionnaires were used – Malnutrition Inflammation Score (MIS) and Dialysis Malnutrition Score (DMS).

The MIS score is structured according to 4 main sections including medical history, physical status, BMI and laboratory parameters. These sections include a total of 10 different components that are divided into four levels of severity – 0 (normal parameter) to 3 (severe abnormality). Accordingly, total score of MIS questionnaire is expressed as sum of all 10 component results, and it ranges from 0-30, with higher score indicating more severe malnourishment and inflammation (58).

The DMS score is divided into seven different parts – dietary habits, weight change, other diseases, fat assessment, muscle wasting, gastrointestinal symptoms and functional capacity. Each of the DMS components can have score that ranges from 1 (normal parameter) to 5 (major severity), with highest score of 35 indicating existence of severely malnourished HD patient.

3.2. Statistical analysis

For statistical analysis of collected data, MedCalc software was used (version 19.1.2, MedCalc Software, Ostend, Belgium). Continuous variables were presented as mean with standard deviation or median with interquartile range, according to normality of data distribution that was assessed with Kolmogorov-Smirnov test. For testing differences between continuous variables, t-test for independent samples and Mann-Whitney test were used. Categorical variables were presented as whole number and percentage, with chi-squared test and Fisher's exact test used to measure differences between groups. Correlation of MIS and DMS score with other parameters was estimated with Spearman's correlation coefficient. Statistical significance in this study was set at $P<0.05$.

4. RESULTS

In this study, a total of 55 HD patients were enrolled, of which 35 men and 20 women. Average age of all included patients was 67.9 ± 11.8 years, without significant differences between men and women (*P*=0.566). Also, groups did not differ in duration of HD treatment as well (*P*=0.290), with average median of 4.0 (2.0-9.0) years for all participants. However, women HD group had significantly longer duration of CKD in comparison with men (11 (6.0-25.5) vs. 33 (10.5-28 years, *P*=0.007). Most frequent venous approach for all participants was arterio-venous fistula (N=31, 56.4 %). Detailed baseline characteristics of all patients are presented in Table 1.

Table 1. Baseline characteristics of study population

Parameter	Men (N=35)	Women (N=20)	Total (N=55)	*P**
Age (years)	68.6 ± 11.8	66.7 ± 12.1	67.9 ± 11.8	0.566
Body weight pre-dialysis (kg)	81.7 ± 13.3	65.9 ± 14.7	75.9 ± 15.7	<0.001
Body weight post-dialysis (kg)	79.7 ± 13.2	63.8 ± 14.5	73.9 ± 15.6	<0.001
Body height (cm)	180.4 ± 7.4	166.7 ± 6.8	175.4 ± 9.8	<0.001
BMI (kg/m^2)	25.1 ± 4.2	23.1 ± 6.5	24.4 ± 5.2	0.026
Waist circumference (cm)	102.0 ± 9.1	93.5 ± 14.4	98.9 ± 11.9	0.025
Hip circumference (cm)	106.6 ± 9.7	102.7 ± 12.1	105.2 ± 10.7	0.196
Duration of CKD (years)	11 (6.0-25.5)	33 (10.5-28)	13 (7-35.75)	0.007
Duration of haemodialysis (years)	4.0 (2-7.75)	7.0 (2-11.5)	4.0 (2.0-9.0)	0.290
Arterial hypertension (N; %)	17 (48.6)	13 (65.0)	30 (54.5)	0.243
Diabetes mellitus (N; %)	3 (8.6)	5 (25.0)	8 (14.5)	0.099
Smokers (N; %)	11 (31.4)	4 (20.0)	15 (27.3)	0.530
Alcohol consumption (N; %)	7 (20.0)	0 (0.0)	7 (12.7)	0.040
Venous approach (N; %)				
Arterio-venous fistula	22 (62.9)	9 (45.0)	31 (56.4)	
Permanent CVC	5 (14.3)	5 (25.0)	10 (18.2)	0.411
Temporary CVC	8 (22.9)	6 (30.0)	14 (25.5)	

Data are presented as mean ± standard deviation, median (IQR) or as whole number (%)
Abbreviations: BMI- body mass index; **CVC-** central venous catheter; **CKD-** chronic kidney disease
* chi-square test/Fisher's exact test or t-test for independent samples/Mann Whitney test

Table 2 reveals the laboratory parameters of the study population. There were no significant differences between the male and female HD group regarding total proteins (*P*=0.675), albumins (*P*=0.636) and all included parameters of lipid panel measurements.

Table 2. Laboratory parameters of study population

Parameter	Men (N=35)	Women (N=20)	Total (N=55)	*P**
Total proteins (g/L)	65.6 ± 4.8	64.0 ± 3.7	65.1 ± 3.9	0.675
Albumins (g/L)	39.1 ± 2.8	38.7 ± 2.5	38.9 ± 2.7	0.636
Total cholesterol (mmol/L)	4.67 ± 4.6	4.67 ± 1.7	4.67 ± 3.8	0.998
Triglycerides (mmol/L)	1.78 ± 1.0	2.2 ± 0.9	1.93 ± 0.9	0.136
LDL-cholesterol (mmol/L)	2.11 ± 0.7	2.58 ± 1.4	2.28 ± 1.03	0.171
HDL-cholesterol (mmol/L)	0.99 ± 0.22	1.1 ± 0.4	1.02 ± 0.3	0.325

Data are presented as mean ± standard deviation
* t-test for independent samples

Regarding questioned eating habits, nobody was adherent to the Mediterranean diet in this population according to guidelines for MDSS (>13.5 total score). Median MDSS score of the HD population was 4.0 (3.0-6.0), with no significant differences between men and women HD group (*P*=0.703). Additionally, none of the 14 included food groups revealed significant differences between men and women in followed eating guidelines for MDSS (*P*>0.05). Patients were most adherent to MDSS guidelines in potato (N=49, 89.1 %) and sweets (N=39, 70.9 %) food groups. Table 3 presents detailed adherence to individual and total Mediterranean diet food groups in the study population.

Table 3. Adherence to individual and total Mediterranean Diet food groups in study population

Parameter	Men (N=35)	Women (N=20)	Total (N=55)	*P*[*]
Cereals (N, %)	13 (37.1)	6 (30.0)	19 (34.5)	0.595
Potato (N, %)	32 (91.4)	17 (85.0)	49 (89.1)	0.656
Olive oil (N, %)	2 (5.7)	1 (5.0)	3 (5.5)	0.998
Nuts (N, %)	0 (0.0)	1 (5.0)	1 (1.8)	0.363
Fresh fruit (N, %)	1 (2.9)	0 (0.0)	1 (1.8)	0.998
Vegetables (N, %)	1 (2.9)	0 (0.0)	1 (1.8)	0.998
Milk and dairy products (N, %)	3 (8.6)	1 (5.0)	4 (7.3)	0.998
Legumes (N, %)	4 (11.4)	2 (10.0)	6 (10.9)	0.998
Eggs (N, %)	9 (25.7)	6 (30.0)	15 (27.3)	0.733
Fish (N, %)	6 (17.1)	3 (15.0)	9 (16.4)	0.998
White meat (N, %)	10 (28.6)	3 (15.0)	13 (23.6)	0.333
Red meat (N, %)	14 (40.0)	10 (50.0)	24 (43.6)	0.476
Sweets (N, %)	23 (65.7)	16 (80.0)	39 (70.9)	0.359
Wine (N, %)	6 (17.1)	0 (0.0)	6 (10.9)	0.358
Total points	4.0 (3.0-6.0)	4.0 (3.0-5.0)	4.0 (3.0-6.0)	0.703[†]

Data are presented as whole numbers (%) or median (IQR)
*chi-square test or Fisher's exact test
†Mann-Whitney test

Body fat assessment revealed that mean percentage was 16.9 ± 5.8 %, with no statistical differences between men and women HD treatment group (16.6 ± 5.1 vs. 17.4 ± 6.9 %, *P*=0.615). Figure 2 presents the body fat percentage according to gender in the total study population.

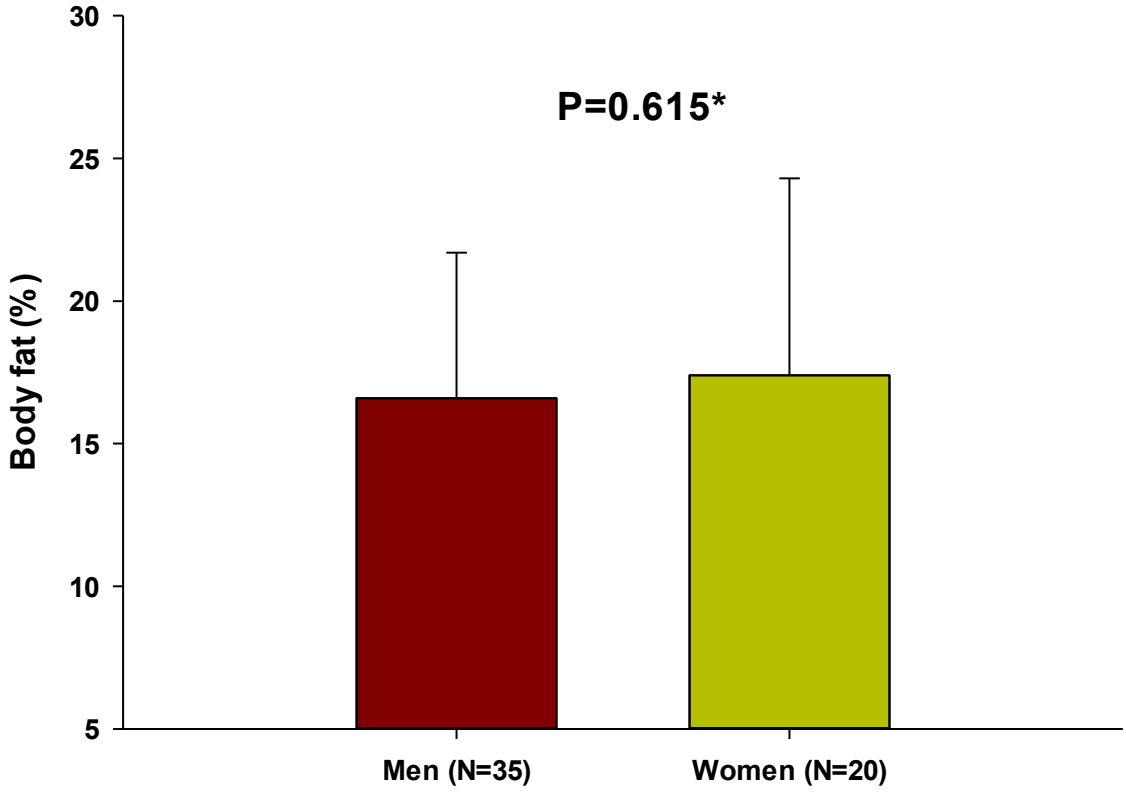

Figure 2. Body fat percentage according to gender in total study population
* t-test for independent samples

Nutrition questionnaires assessment revealed that men HD group had significantly lower MIS total score in comparison with women HD group (5 (3-7) vs. 7 (5-9.5), *P*=0.038) (Figure 3A). However, there was no statistical differences in DMS total score between men and women HD group (*P*=0.202) (Figure 3B), with median of overall population of 12 (10-14).

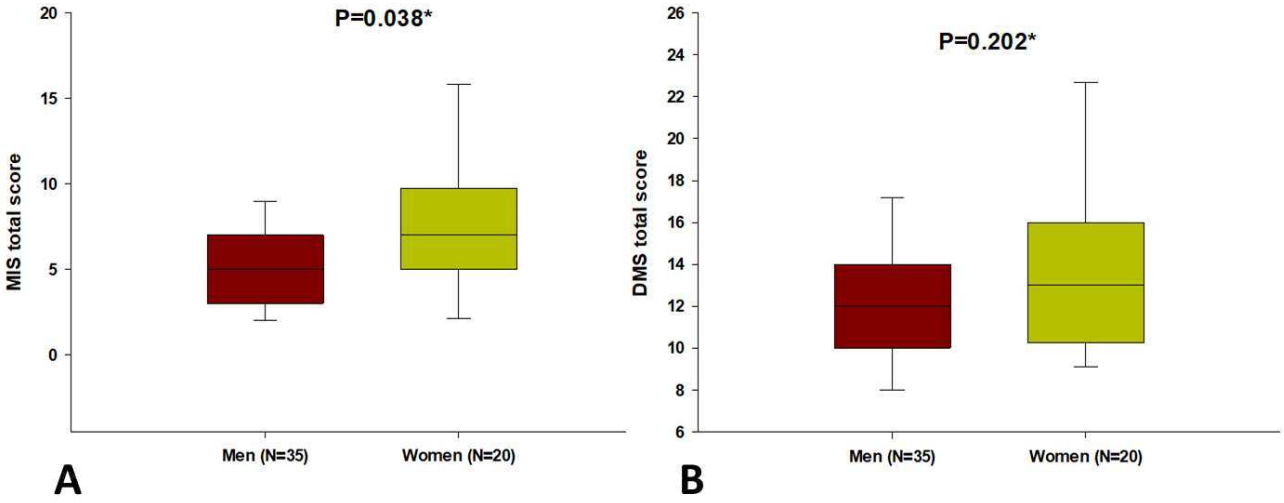

Figure 3. Total MIS score (A) and DMS score (B) according to gender in study population
Abbreviations: MIS- Malnutrition Inflammation Score; **DMS**- Dialysis Malnutrition Score
* Mann-Whitney test

Correlation analysis between nutritional scores with other parameters revealed significant negative correlation of MIS and DMS scores with BMI (r=-0.498, *P*<0.001; r=-0.499, *P*<0.001, respectively) and waist circumference (r=-0.432, *P*=0.001; r=-0.318, *P*=0.018, respectively). Additionally, there was a significant positive correlation between DMS score and duration of HD treatment (r=0.433, *P*<0.001). There was no significant correlation between MIS and DMS score and the remaining parameters (Table 4).

Table 4. Correlation analysis between total MIS and DMS points and different parameters in total study population (N=55)

Parameter	MIS score r*(*P*)	DMS score r*(*P*)
Age (years)	0.119 (0.385)	0.184 (0.178)
BMI (kg/m^2)	-0.498 (<0.001)	-0.499 (<0.001)
Waist circumference (cm)	-0.432 (0.001)	-0.318 (0.018)
Duration of CKD (years)	0.211 (0.122)	0.235 (0.084)
Duration of haemodialysis (years)	0.250 (0.065)	0.433 (<0.001)
Total proteins (g/L)	-0.174 (0.202)	-0.031 (0.820)
Albumins (g/L)	-0.220 (0.106)	-0.125 (0.365)
Total cholesterol (mmol/L)	0.130 (0.344)	0.024 (0.863)
Triglycerides (mmol/L)	0.006 (0.965)	-0.080 (0.563)
LDL-cholesterol (mmol/L)	-0.048 (0.726)	-0.093 (0.501)
HDL-cholesterol (mmol/L)	0.166 (0.226)	0.130 (0.343)
Total MDSS points	-0.060 (0.664)	-0.046 (0.741)

Abbreviations: MIS- Malnutrition Inflammation Score; **DMS**- Dialysis Malnutrition Score; **MDSS**- Mediterranean Diet Serving Score; **BMI**- body mass index
*Spearman's correlation coefficient

Furthermore, there was a significant negative correlation between body fat percentage and total MIS score (r=-0.270, *P*=0.046) (Figure 4A), and DMS score as well (r=-0.328, *P*=0.015) (Figure 4B).

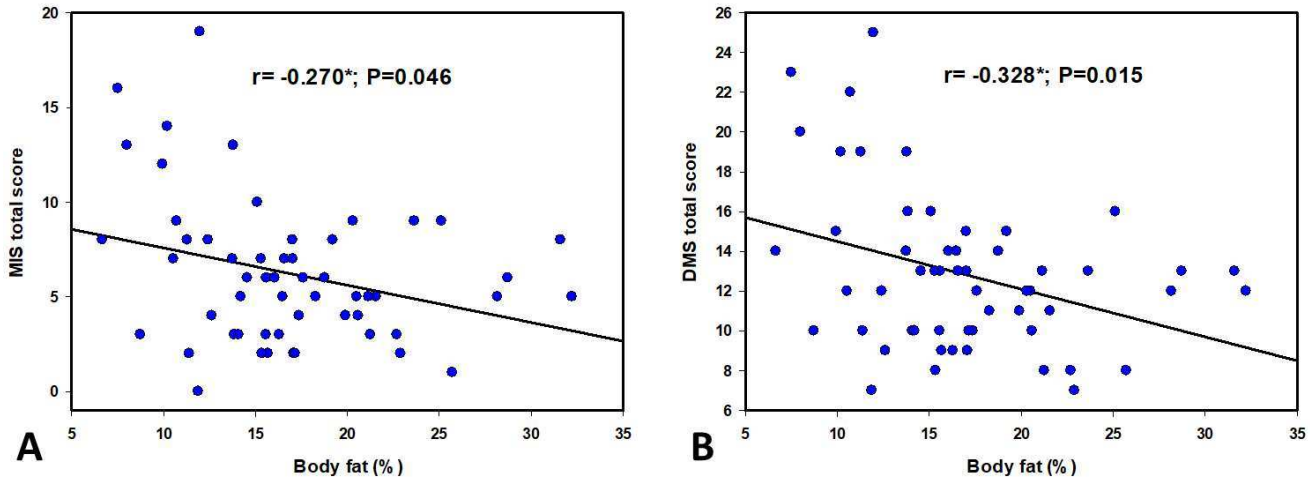

Figure 4. Correlation analysis between body fat percentage and total MIS score (A) and DMS score (B) in total study population (N=55)
Abbreviations: MIS- Malnutrition Inflammation Score; **DMS**- Dialysis Malnutrition Score
* Spearman's correlation coefficient

5. DISCUSSION

The main finding of the presented study was that the BMI and body fat percentage negatively correlated with the MIS and the DMS in patients on HD. This finding was further supported by a negative correlation between the waist circumference and the MIS and DMS. This observation has also been reported by previously released studies. The prediction of malnutrition in patients on HD is established via variable screening tools and scoring methods by clinicians (59). However, the majority of these methods are not applicable in daily practice (59). BMI appears useful as an important component of multiple malnutrition screening tools, whereas in state of global chronic energy deficiency BMI may not have an adequate value in assessing malnutrition (59). Anthropometric measurements, such as waist circumference, weight and BMI provide satisfactory information about nutritional status and prognosis for patients suffering from chronic disease (60). Janardhan et al. have encouraged that the DMS negatively correlated with anthropometric measurements such as body weight (59). Furthermore, the triceps skin fold thickness, a measure of body fat content, was an additional parameter negatively correlated with the DMS (59). A study by Kalantar-Zadeh et al. found that the DMS was significantly correlated with anthropometric parameters such as BMI (61). It is worth noticing that a study by Brandao da Cunha Bandeira et al. found the BMI to be an important independent variable of the MIS (62).

In our study, women had a slightly higher percentage of body fat which was not statistically significant. However, women on average had a significantly longer duration of HD and a lower BMI. Since the duration of HD positively correlated with the DMS, our study suggests that women on HD may be more prone to malnutrition than men. This was supported by our study because women on HD had a significantly higher MIS and DMS than men, but the DMS difference was not significant. However, this finding should be carefully interpreted. Interestingly, Espahbodi et al. indicated an association between patients´ sex and malnutrition states in ESRD patients (63). In their study all women, but not men had some degree of malnutrition (63). Furthermore, a study conducted by Farrokhi et al. demonstrated that malnutrition was significantly more frequent in females on chronic HD (64).

A further finding of our study was that biochemical markers such as albumin, total proteins, total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol may not generally be in accordance with the clinical picture of malnourished patients on HD since they were in the normal reference range. This observation has been supported by Lawson et al. who have shown that serum albumin failed to identify patients with a significant reduction in anthropometric measurements and thus found a clinical assessment to be essential (65).

Contrary to this finding, Janardhan et al. reported that biochemical markers such as serum albumin are reliable and clinically applicable measures of protein-energy status in patients on HD (59). The same study states that this screening tool has to be interpreted carefully because certain non-nutritional conditions such as inflammation can significantly impair the reliability and accordance of this marker with the clinical picture of malnutrition (59). Additionally, Janardhan et al. demonstrated that serum cholesterol is a convenient screening tool in the detection of chronic protein-energy malnutrition states in patients undergoing hemodialysis (59). In addition, a study by Espahbodi et al. suggested that biochemical markers such as albumin and cholesterol were not significantly associated with malnutrition and thus did not provide reliable information about the nutritional status in patients on hemodialysis (63).

Further on, our study reports that none of the subjects were adherent to the Mediterranean diet according to guidelines for MDSS (<13.5 total score). Our studied patient population mainly consumed potatoes, cereals, eggs, red meat and sweets and did not fulfill the total score required by the criteria of the MDSS for adherence to the Mediterranean diet. A study by Chaveau et al. has evidenced that the Mediterranean diet has various beneficial effects on inflammation and renal function in CKD patients (66). It is worth mentioning that there is no single dietary component responsible for an improved clinical picture of the patients´ conditions, but instead the introduction of a balanced diet can positively influence on the patients´ condition (66). This is due to a decreased production of waste products which are crucial for the outcome hemodialysis (66). Furthermore, their study has shown that fruits and vegetables, dairy products and white meat are recommended to be consumed regularly (66). High quality, nutrient-dense carbohydrates coming from fruits, vegetables, whole grains and legumes have a low glycaemic index which decreases oxidative stress and inflammation in dialysis patients (66). In our study patients had a low consumption of fruits and vegetables, white meat, legumes and dairy products. Therefore, the diet of our population might not have been favorable for their overall condition and nutritional status.

It should be acknowledged that our study, however, has some limitations. Firstly, our study included only a small number of participants that were unequally divided into two men and women HD groups. Moreover, the study was performed as a single center study and involved only patients treated at the Department of Nephrology, University Hospital of Split. Furthermore, some of the collected data could be influenced by recall, and therefore be susceptible to false presentation.

CKD patients on HD are frequently affected by chronic protein-energy malnutrition states (32). In this patient population it is critical to ensure an adequate intake of high-quality nutrients which is essential for maintenance of dialytic stability (67). These patients require sufficient intake of calories, protein, electrolytes and water (67). This is crucial for obtaining favorable dialytic results, survival rates and quality of life in patients undergoing long-term hemodialysis (67). Therefore, further research is needed to more closely investigate the topic.

6. CONCLUSION

1. Patients on HD had a low adherence to Mediterranean diet.

2. Patients on HD had high MIS and DMS scores.

3. There was a significant negative correlation between MIS and DMS scores with body fat percentage in patients on HD treatment.

4. Women had significantly higher MIS score in comparison with men on HD.

5. There were no statistical differences between percentage of body fat and DMS scores in men and women on HD treatment.

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8. SUMMARY

Objectives: The main objectives of this study were to assess nutritional status and adherence to Mediterranean diet in patients on hemodialysis treatment.

Materials and methods: The study included the 55 patients (35 men and 20 women) on hemodialysis (HD) treatment for at least 6 months that were older than 18 years. Venous blood samples were taken for evaluation of laboratory parameters. All study subjects underwent physical examination and anthropometric measuring. After taking the anamnestic data, information regarding Mediterranean diet adherence was collected using Mediterranean Diet Serving Score (MDSS) questionnaire. During clinical examination, all patients underwent caliper skin folds measuring for body fat percentage estimation. Nutritional status was assessed using Malnutrition Inflammation Score (MIS) and Dialysis Malnutrition Score (DMS).

Results: Average age of all included patients was 67.9 ± 11.8 years, without significant differences between men and women (P=0.566). However, women HD group had significantly longer duration of chronic kidney disease in comparison with men (P=0.007). There was no significant difference in any of the laboratory parameters in the different groups of the study population. None of the patients was adherent to the Mediterranean diet in the study population according to the guidelines for MDSS. Women HD group presented with a significantly higher MIS score when compared with men (P=0.038), while body fat assessment revealed that mean percentage of total HD population was 16.9 ± 5.8 %, with no statistical differences between men and women. Correlation analysis between nutritional scores with other parameters revealed significant negative correlation of MIS and DMS scores with BMI (P<0.001) and waist circumference (P=0.001 and P=0.018, respectively). Also, there was a significant positive correlation between duration of HD and DMS score (P<0.001). Finally, there was a significant negative correlation between body fat percentage and total MIS score (P=0.046), and DMS score as well (P=0.015).

Conclusion: Patients on HD had low adherence to Mediterranean diet, and high MIS and DMS malnutrition scores which negatively correlated with estimated body fat percentage. More studies are needed to further clarify connection between these parameters.

9. CROATIAN SUMMARY

Naslov diplomskog rada: Procjena nutritivnog statusa i prehrambenih navika u pacijenata na liječenju hemodijalizom.

Cilj: Glavni ciljevi ove studije su bili procijeniti nutritivni status i stupanj pridržavanja mediteranskom tipu prehrane u pacijenata na hemodijalizi.

Ispitanici i metode: Studija je obuhvatila ukupno 55 pacijenata (35 muškaraca i 20 žena) na hemodijalizi (HD) u trajanju od najmanje 6 mjeseci, starijih od 18 godina. Uzorci venske krvi su prikupljeni za određivanje laboratorijskih parametara. Svi ispitanici su klinički pregledani, te su im izmjerene antropometrijske značajke. Ispitane su informacije o pridržavanju mediteranskom tipu prehrane pomoću MDSS (engl. *Mediterranean Diet Serving Score*) upitnika. Tijekom kliničkog pregleda, svi su pacijenti podvrgnuti mjerenju debljine nabora kože radi procjene postotka tjelesne masti. Nutritivni status procijenjen je uporabom MIS-a (engl. *Malnutrition Inflammation Score*) i DMS-a (engl. *Dialysis Malnutrition Score*) upitnika.

Rezultati: Prosječna dob svih uključenih bolesnika bila je 67,9 ± 11,8 godina, bez značajnih razlika između muškaraca i žena (P=0,566), dok su žene imale su znatno duže trajanje kronične bolesti bubrega u usporedbi s muškarcima (P=0,007). Nije bilo značajne razlike u bilo kojem od laboratorijskih parametara u različitim skupinama ispitivane populacije. Nijedan uključen pacijent nije se pridržavao mediteranskom tipu prehrane prema MDSS smjernicama. Žene su pokazale značajno veći MIS rezultat u usporedbi s muškarcima (P=0,038), dok je procjena tjelesne masnoće pokazala da je prosječni postotak ukupne populacije bio 16,9 ± 5,8 %, bez statističkih razlika između muškaraca i žena. Korelacijska analiza rezultata upitnika s ostalim parametrima pokazala je značajnu negativnu povezanost MIS i DMS bodova s indeksom tjelesne mase (P<0,001 za oboje) i opsegom struka (P=0,001 i P=0,018). Također, postojala je značajna pozitivna korelacija između trajanja liječenja i DMS rezultata (P<0,001). Na kraju, pronađena je značajna negativna korelacija između postotka tjelesne masnoće i ukupnog MIS (P=0,046), te DMS-a (P=0,015).

Zaključci: Pacijenti na liječenju hemodijalizom imali su nisku stopu pridržavanja mediteranskom tipu prehrane, te visoke MIS i DMS vrijednosti, koji su negativno korelirali s procijenjenim postotkom tjelesne masti. Potrebno je provesti daljnje studije koje bi dodatno razjasnile povezanost između navedenih parametara.

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