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Association of cardiometabolic risks with body composition in hemodialysis patients

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Abstract. – OBJECTIVE: High body fat ratio is known as one of the main reasons that increase the risk of cardiovascular disease. This study examined the relationship between body composition and cardiometabolic risks in hemodialysis (HD) patients.

PATIENTS AND METHODS: This study was conducted with chronic kidney disease (CKD) patients who received HD treatment between March 2020 and September 2021. Anthropometric measurements of the individuals and their body composition analyses were performed using the bioelectrical impedance analysis (BIA) method. Framingham risk scores were calculated in order to determine the cardiometabolic risk factors of individuals.

RESULTS: According to the Framingham risk score, 15.96% of individuals were found to have a high cardiometabolic risk. The lean-fat tissue index (LTI)/(FTI), body shape index (BSI) and visceral adiposity index (VAI) (female-male) values of individuals with high risk according to the Framingham risk score were found to be 11.34±2.29, 13.52±2.88, 8.50±3.89, 9.60±3.07, 0.086±0.024, respectively. The effect of anthropometric measurements in estimating the Framingham risk score was examined using the linear regression analysis. The regression analysis performed with BMI, LTI, VAI values, it was determined that 1-unit increase in VAI increased the Framingham risk score by 1,468 units (OR: 0.951-1.952) (*p*=0.002).

CONCLUSIONS: It has been discovered that indices indicating adipose tissue increase the Framingham risk score in HD patients, independent of BMI. It is recommended to evaluate the ratios showing body fat ratio in cardiovascular diseases.

Key Words:
Cardiometabolic risks, Hemodialysis, Framingham risk score, Fat tissue, Lean tissue.

Introduction

Chronic kidney disease and cardiovascular disease are clinical disorders that are closely related with each other[1]. It is observed that hemodialysis (HD) patients have an increased risk of mortality related to cardiovascular diseases in general. It is underlined that hemodialysis patients commonly experience atherosclerosis and coronary artery diseases. The incidence of myocardial infarction (MI), congestive heart failure, sudden death, and arrhythmia were discovered to be greater in HD patients than in the general population[2]. Age, gender, hypertension, obesity, dyslipidemia, and smoking increase the risk of cardiovascular disease and, consequently, the risk of death in HD patients. Among the factors that increase the cardiovascular risk, the increase in body fat ratio is highlighted in particular[3,4]. An increase in body fat increases the risk of mortality in HD patients and in the general population since body fat rate can increase inflammation[5]. Many studies[6-8] have shown that there is a positive correlation between body fat ratio and cardiovascular diseases. On the other hand, the preservation of lean tissue and certain levels in HD patients may reduce mortality in individuals. In randomized controlled studies[9-11], the importance of body composition rather than high BMI levels in determining the cardiac risk of HD patients is stressed. When examining body composition, the distribution of muscular tissue and adipose tissue is particularly significant. Patients with HD require anthropometric measurements, which are not affected by the change in body fluid amount. In addition to BMI, indices, such as VAI, FTI, LTI and BSI have recently gained prominence[12,13].

In this study, body composition in HD patients was evaluated with various indices and its effect on cardiometabolic risk was investigated. In this context, it is aimed to determine the relationship with the Framingham risk score by calculating BMI, VAI, FTI, LTI and BSI.

Patients and Method

Study Population and Ethical Procedures

This study was conducted with CKD patients who received HD treatment in Malatya Tur-

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gut Ozal University, hemodialysis unit between March 2020 and September 2021. Patients receiving hemodialysis treatment regularly (3 days a week) were included in the study. The study was conducted in compliance with the Helsinki-2013 declaration at every stage. The study protocol was approved by the local ethics committee.

Inclusion Criteria for the Study

Patients between 18-80 years of age, diagnosed with CKD by a nephrologist, undergoing hemodialysis treatment, regularly receiving hemodialysis treatment [urea reduction rate (URR) should be minimum > 65%, minimum Kt/V= 1.2], who will be able to answer the study questions, with healthy mental condition were included in the study.

Exclusion Criteria from the Study

In addition to the diagnosis of chronic kidney failure, individuals with diseases such as cancer, liver failure, advanced heart failure, Type 1 diabetes, those under the age of 18 and over the age of 80, patients who cannot feed on their own, and whose mental condition is not suitable enough to answer the study questions were not included in the study.

Body Composition

Body weights and heights of the individuals were measured with light clothing and without shoes. Body analysis of individuals was performed using a TANITA BC545N series with bioelectronic impedance analysis (BIA) technology, an accuracy of 0.1 kg and a maximum capacity of 150 kg (Type BC545N, Tokyo, Japan). Individuals' height was measured using a portable stadiometer with an accuracy of 0.1 cm, and their waist circumference was measured using a tape measure that extended to the navel to within 0.1 cm (SECA 264, Seca Gmbh and Co, Hamburg, Germany). Body Mass Index was calculated by dividing the body weight (kg) by the square of the height (m). As stated in the ERA-EDTA and ISRNM guidelines, BMI lower than 23 kg/cm^2 was considered as a sign of malnutrition[14]. The BIA gadget was used to determine body composition. Electrodes were put on the nondominant side of the body's hand and foot while the patient was supine, and the results were available in 2 minutes. The BIA analyzes electrical responses at 50 distinct frequencies between 5 and 500 kHz to determine body composition. By fitting a polynomial curve known as the Cole-Cole plot with numerous frequencies, theoretical resistance values at zero and infinite frequencies can be calculated. The graphic representation of the curve can be used to examine the measurement's validity. The study only included participants who had at least one valid BCM measurement.

Adiposity and Indices

Visceral Adiposity Index (VAI)

VAI is a sex-specific index based on WC, BMI, TG, and HDL-C, and estimates the visceral adiposity functionality. The VAI was calculated as follows: (TG and HDL-C were in mmol/l and WC in cm).

Calculation of VAI for men: (WC / [39.68 + (1.88*BMI)]) * (TG /1.03) * (1.31 /HDL-C).

Calculation of VAI for women: (WC / [36.58 + (1.89* BMI)]) * (TG/0.81) * (1.52 / HDL-C).

Waist circumference (WC) = cm, Triglyceride (TG) and High-Density Lipoprotein Cholesterol (LDL-C) = mmol/l)[15].

Lean and fat tissue indices

Input parameters included the patient's age, sex, height, and weight. Muscle mass was expressed as the lean tissue mass or lean tissue index (LTI) and fat mass or fat tissue index (FTI). Lean tissue index (LTI)=Body lean mass/Height^2, Fat tissue index (FTI)= Body fat mass/Height^2)[16].

Biochemical Measurements

Morning fasting (at least 12 hours fasting) venous blood and fasting serum glucose, total cholesterol, high-density lipoprotein-cholesterol (HDL-C), low-density lipoprotein-cholesterol (LDL-C), very low-density lipoprotein-cholesterol and triglyceride levels were measured. After 10 minutes of centrifugation at 1000 rpm, the upper layer of the serum was taken into the centrifuge tube (Scientific Industries Inc., Bohemia, NY, USA). All blood samples were stored in a -80 °C refrigerator until laboratory analysis.

Calculation of Cardiometabolic Risk Status

The Framingham risk scores of the patients were calculated according to their age. Calculations were made by taking into account gender, smoking status, systolic blood pressure, total cholesterol, HDL cholesterol, presence of diabetes diagnosis, drug use for hypertension and presence of vascular disease. For the calculation, 'Framingham Risk Score calculation web address' was used.

Individuals who have been smoking regularly for the last 1 year are included in the 'having a habit of smoking' group. After a 5-minute break, the blood pressure of each individual was measured by an experienced medical professional.

Total cholesterol and HDL cholesterol levels in serum were tested using routine laboratory procedures. The intersection values were used for both cholesterol levels. Total cholesterol is evaluated between the values <160, 160-199, 200-239, 240-279 and >280 mg/dL, while HDL cholesterol is evaluated between the values <35, 35-44, 45-49, 50-59, >60 mg/dL, respectively.

Diabetes mellitus was diagnosed based on a fasting blood glucose level of 126 mg/dL or above or the use of oral antidiabetic medications. Similarly, the regularity of hypertension medication use was questioned. Individuals were questioned as to whether or not they had previously been diagnosed with cardiovascular diseases and MI.

The risk calculated in the Framingham risk score is the percentage risk of death from cardiovascular diseases within 10 years. According to the Framingham risk score results, individuals with 10% or less risk are in the "Low Risk" group, individuals between 10-20% are in the "Moderate Risk" group, and individuals above 20% are in the "High-Risk" group, respectively.

Statistical Analysis

The data obtained in the study were analyzed using the Statistical Package for the Social Sciences (SPSS) 22.0 (IBM Corp., Armonk, NY, USA) program. All analyses had a significance level of $p<0.05$. The conformity of the variables to the normal distribution was examined using the Shapiro-Wilk test. When summarizing the variables, mean±standard deviation values are presented as descriptive statistics. Correlation analysis was performed with the Spearman correlation test for non-parametric data. According to the Framingham risk score intersection points, individuals were separated, and evaluations were performed accordingly. According to the Framingham risk score results, individuals with 10% or less risk are in the "Low Risk" group, individuals between 10-20% are in the "Moderate Risk" group, and individuals above 20% are in the "High-Risk" group, respectively. Using a multivariate linear regression model, the independent effects of different predictors on the Framingham risk score were examined.

Results

Table I lists the general characteristics of the individuals who participated in the study. Women constituted 47.34% of the individuals participated in the study. The mean age of the individuals and the age at diagnosis of CKD were found to be 56.21±11.22 and 14.28±3.48 years, respectively. The individuals of 34.04% were determined to be smokers. The mean BMI value of the individuals was found to be 26.22±5.06 kg/cm^2 and the BMI value of 29.26% of the individuals was found below the recommended range. The rate of individuals doing regular physical activity was determined to be 23.94%, while the rate of individuals doing regular physical activity 3 days a week was 11.70%. It was determined that the rate of individuals who applied medical nutrition therapy according to their disease status was 52.13%. According to the Framingham risk score, the rate of individuals with high cardiometabolic risk was 15.96%.

Table I. General characteristics of individuals.

Variables	n (%)
Female	89 (47.34)
Male	99 (52.66)
Age (years) (±SD)	56.21±11.22
CRF diagnosis time (years) (±SD)	14.28±3.48
Dialysis age (years) (±SD)	8.01±2.24
Smoking status	64 (34.04)
BMI (kg/m^2) (±SD)	26.22±5.06
BMI classification (kg/m^2)	
Underweight (<23.00)	55 (29.26)
Normal (23.00-25.00)	76 (40.43)
Overweight (25.01-30.00)	48 (25.53)
Obese (>30)	9 (4.79)
Regular physical activity status (30 minutes)	
Yes	45 (23.94)
No	143 (76.06)
Frequency of physical activity a week	
1-2 days a week	18 (9.57)
3 days in a week	22 (11.70)
4 and upper days a week	5 (2.66)
Medical nutrition therapy practice status	
Yes	98 (52.13)
No	90 (47.87)
Framingham risk score (%)	
Low Risk (< 10%)	81 (43.09)
Moderate Risk (10-20%)	77 (40.96)
High risk (>20%)	30 (15.96)

CKD; Chronic kidney disease, BMI; Body mass index. $\bar{x}$ ± SD: mean±standard deviation.

Table II. Blood pressures and laboratory findings of HD patients according to Framingham risk score.

Blood pressures and laboratory findings	Low Risk n=81 x̄ ± SD	Moderate Risk n=77 x̄ ± SD	High Risk n=30 x̄ ± SD	*p*
Systolic blood pressure (mm Hg)	117.34±13.11	129.85±12.27	134.10±14.44	0.004*
Diastolic blood pressure (mm Hg)	85.91±8.04	88.40±7.25	87.21±9.02	0.008
Total cholesterol (mg/dl)	201.81±30.70	227.66±33.97	228.55±41.77	0.022
HDL-cholesterol (mg/dl)	46.34±12.31	41.12±10.89	31.54±13.91	0.091
LDL-cholesterol (mg/dl)	119.43±33.53	135.34±35.33	141.18±35.54	0.088
VLDL-cholesterol (mg/dl)	20.56±11.23	43.46±36.31	31.76±23.23	0.041
Triglyceride (mg/dl)	98.14±62.67	196.14±98.14	223.67±84.90	0.012
Glucose (fasting) (mg/dl)	89.61±12.21	137.21±68.83	116.66±47.65	0.009

**According to the Framingham risk score results, individuals with 10% or less risk are in the "Low Risk" group, individuals between 10-20% are in the "Moderate Risk" group, and individuals above 20% are in the "High-Risk" group, respectively. x̄ ± SD: mean±standard deviation.

The blood pressures and laboratory findings of the individuals according to the Framingham risk score are presented in Table II. According to the Framingham risk score, individuals in the high-risk group had higher mean systolic blood pressure (SBP), total cholesterol, VLDL cholesterol and triglyceride levels compared to the other groups ($p<0.05$).

Anthropometric measurements of individuals according to Framingham Risk Score are given in Table III. Individuals with a high Framingham risk score had higher mean BMI and FTI in both men and women. Visceral adiposity index was found to be higher in both men and women with a high Framingham risk score ($p<0.05$).

In the regression analysis performed to predict the cardiometabolic risk in hemodialysis patients, VAI, BMI (kg/m^2) and FTI were found to have a significant relationship in estimating the Framingham risk score (Table IV). The Framingham risk score was increased by 1.468%, 1.9588% and 1.3466%, respectively, when the VAI, BMI (kg/m^2) and FTI values were increased by 1-fold. BMI (kg/m^2) was found to have the greatest effect on the estimation of the Framingham risk score ($p<0.05$).

Discussion

In this study, the effects of BMI and other indices showing body composition on cardiometabolic risks in patients receiving regular HD therapy were investigated. It has been demonstrated that VAI, BMI and FTI increase cardiometabolic risk. Many studies[11-14] have shown that increased cardiometabolic risk is associated with mortality in HD patients.

It was revealed that hemodialysis patients have a greater risk of cardiovascular disease-related death. Cardiovascular system in HD patients is affected by many factors such as increased oxidative stress and insufficient antioxidant intake[12,17,18]. In the study of Jo et al (2017)[19] it was found that ESRD was seen at similar rates in both genders.

Table III. BMI and anthropometric measurements of individuals according to Framingham Risk Score.

BMI and anthropometric measurements	Low Risk n=81 x̄ ± SD	Moderate Risk n=77 x̄ ± SD	High Risk n=30 x̄ ± SD	*p*
BMI (kg/m²)	22.03±5.69	26.35±8.21	29.01±7.11	0.039
LTI	11.07±2.16	12.32±2.05	11.34±2.29	0.029
FTI	12.09±2.19	12.47±3.52	13.52±2.88	0.007
VAI (male)	5.09±3.04	6.72±3.09	8.50±3.89	0.002
VAI (female)	6.06±3.34	7.02±3.97	9.60±3.07	0.002
BSI	0.073±0.011	0.097±0.015	0.086±0.024	0.048

BMI; Body mass index, LTI; Lean tissue index, FTI; fat tissue index, BSI; Body shape index, VAI; viseral adiposity index. x̄ ± SD: mean±standard deviation.

Table IV. Results of linear regression analysis with anthropometric measurements to predict cardiometabolic risk in hemodialysis patients.

Variables	OR	95% CI	*p*
VAI	1.468	0.951-1.952	**0.002**
BMI (kg/m²)	1.958	1.915-4.228	**0.043**
FTI	1.346	1.003-2.641	**0.005**

BMI; Body mass index., LTI; Lean tissue index., FTI; Fat tissue index., VAI; Viseral adiposity index, OR; Odds ratio, ($p<0.05$) is accepted as statistically significant.

In another study[20], it was determined that the average age of hemodialysis patients was 50 or older, while the average age of CKD diagnosis was 10 or older. In this study, it was observed that the gender distribution of the individuals included in the study was close to each other and the average age was found to be 50 years and above.

The increased oxidative stress in hemodialysis patients increases the prevalence of cigarette smoking. Two randomized, controlled studies[5,17] found that hemodialysis patients who smoked had a shorter life expectancy and a higher risk of cardiovascular disease. The CRP value, a sign of inflammation, was found to be increased, particularly in smokers. In this study, it was determined that the rate of individuals who smoked was higher than the other two studies.

According to many studies[16-18], physical activity improves the life expectancy of hemodialysis patients and protects them from many diseases. However, many studies[19,21] have shown that hemodialysis patients are physically inactive compared to healthy individuals. In this study, regular physical activity (minimum 30 minutes) was examined. Less than 25% of the individuals included in the study stated that they had a regular physical activity, and it was seen that, and their frequency of weekly physical activity, it was significantly below the World Health Organization's recommendation (150 minutes per week).

Cardiovascular disease is substantially related with atherosclerosis and chronic inflammation in patients taking long-term HD treatment[22]. In HD patients, increased cardiometabolic risks increase the risk of cardiovascular disease[23]. Compared to the general population, cardiovascular disease is the leading cause of death in HD-treated patients; nonetheless, cardiovascular disease is associated with a significantly higher risk of mortality[24,25]. According to the findings of studies[26] of the general population, an increase in BMI, WC and WHR increases the risk of death. However, there are also studies[27] showing that the prognostic value of obesity measures, including BMI, WC and WHR, is inversely related to mortality in CKD patients receiving HD treatment. For example, some studies[28-30] have identified an inverse relationship between BMI and all-cause mortality (described in the context of reverse epidemiology), while others have found no correlation between BMI and all-cause mortality[31]. Apart from subcutaneous adipose tissue, abdominal adipose tissue measured by waist circumference has been shown to increase the risk of cardiovascular mortality in HD patients[32,33]. However, waist circumference was also found to be associated with BMI and body weight. In addition, it is underlined that BMI and regular clinical assessment are insufficient for assessing cardiometabolic risk. In order to better comprehend the association between morbidity and mortality of anthropometric measurements in HD patients, it is noted that further research is necessary, and that more validated and accurate anthropometric metrics are required[34]. Especially the measurements that are not affected by the increased fluid accumulation in the tissues draw attention. It was determined that recently developed VAI, FTI and LTI measurements were more sensitive than other anthropometric measurements. As previously stated, more validated and reliable anthropometric parameters are needed[35]. In the general population, the relationship between VAI, FTI, LTI and mortality was investigated[36]. There is no published research addressing the cardiometabolic risk associated with these parameters in hemodialysis patients. In this study, the correlations between cardiometabolic risk and anthropometric variables were examined in detail. Individuals with a high cardiometabolic risk have been reported to have VAI, FTI and BMI values. The muscle tissue index was shown to be lowest in the group with the highest cardiometabolic risk. This indicates that the cause of weight gain in HD patients is adipose tissue. The increase in adipose tissue, especially when it increases in the waist circumference, causes inflammation, and may increase the cardiometabolic risk.

Risk factors such as malnutrition and increased inflammation increase oxidative stress in HD patients. There are many causes of increased inflammation in HD patients. Examples include nutrition, body composition (imbalance between muscle and fat tissue), and an increase in blood urea uric acid levels. In this study, it was observed that there was a positive and strong correlation between cardiometabolic risk and VAI. The increase of adipose tissue around the waist can potentially increase the inflammatory markers and increase the cardiometabolic risk. A large-scale study of 27,098 participants from 52 countries showed a gradual and highly significant association between WHR and MI after adjusting for other CAD risk factors[36,37]. Furthermore, a recent study[37] indicated that people with a larger waist circumference had lower survival rates than those with a higher BMI. Increases in waist circumference and adipose tissue have been reported to be related with MI in CKD patients in stages 3 and 4 who fit the metabolic syndrome criteria[38]. In a study of individuals with end-stage renal disease, waist circumference was found to increase cardiovascular mortality in Cox models where BMI was kept constant[39]. In the linear regression model made in this study, it was observed that VAI was the component that increased the cardiometabolic risk the most.

Limitations

The number of samples in the study and obtaining data from a single center are among the limitations of the study. Another important limitation is the difficulties of taking measurements with a body analyzer in hemodialysis patients. It can be defined as an imbalance of Na/K in the body.

Conclusions

Multiple factors increase the cardiometabolic risk in HD patients. There is no anthropometric measurement in the literature that indicates cardiometabolic risk. It is stated that an increase in adipose tissue in particular, may increase the cardiometabolic risk. In this study, the effects of FTI, VAI, LTI and BSI on the Framingham score, which signals cardiometabolic risk, were examined in HD patients. VAI and FTI were found to be effective in predicting cardiometabolic risk. It is thought that the increase in tissue caused by adipose tissue in HD patients will invite cardiovascular diseases and cause an increase in CAD-related mortality.

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Ethics Approval

The study was conducted with the approval of Malatya Turgut Ozal University Ethics Commission dated 17/11/2022 number 362. The study was carried out in accordance with the Helsinki Declaration 2013.

Informed Consent

Written informed consent was obtained from all individuals participating in the study.

Availability of Data and Material

All data of the study can be accessed through the corresponding author upon reasonable request.

Conflict of Interest

The author has no conflicts of interest to declare.

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