ORIGINAL ARTICLE

DETERMINATION OF THE RISK OF CORONARY HEART DISEASE WITH FRAMINGHAM RISK SCORE IN CHRONIC KIDNEY DISEASE PATIENTS

Kronik Böbrek Hastalarında Framingham Risk Skoru İle Koroner Kalp Hastalığı Riskinin Belirlenmesi

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ABSTRACT

Objective: The role of the Framingham risk score in predicting coronary artery risk in chronic kidney disease patients and its relationship with atherosclerosis in the abdominal aorta will be examined. The usability of the Framingham risk score as a criterion when deciding on cardioprotective treatment will be evaluated.

Material and Methods: One hundred twenty individuals with chronic kidney disease were included. Sociodemographic data, medical history, and treatments were recorded. Lipid levels, creatinin levels and calculated glomerular filtration rate (GFR) levels were recorded. Radiologic images were examined. Framigham risk scores were calculated. Data were analyzed in SPSS, $p<0.05$ was taken as the significance criterion.

Results: When Framigham risk scores of the individuals were evaluated, 36 (30%) were low, 52 (43.3%) were moderate, and 32 (26.7%) were high. Framigham risk score was found to be higher as GFR decreased ($X^2=36.78$ p=0.001*). No reduction in cardiovascular risk was observed with renal replacement therapy in stage 5 chronic renal disease. When the lipid profile was evaluated; high density lipoprotein (HDL) levels were inversely associated with Framingham risk scores and more correlated with stage. HDL levels were significantly lower as coronary risk increased. Framingham risk score was higher in individuals with intravascular calcification. The sensitivity of the score was found to be high in indicating cardiovascular risk in chronic kidney disease. ($X^2=15.03$; P=0.001*)

Conclusion: Framingham risk score can be used as a reliable tool to determine atherosclerosis and cardiovascular risk in patients with chronic kidney disease and to decide on cardioprotective treatment, especially in the patient group where invasive methods cannot be used.

Keywords: *Chronic Kidney Disease; Framingham Risk Score; Cardiovascular Risk*

ÖZET

Amaç: Kronik böbrek hastalarında koroner arter riskini öngörmede Framingham risk skorunun yeri ve abdominal aortadaki aterosklerozla ilişkisi incelenecektir. Kardiyoprotektif tedaviye karar verirken Framingham risk skorunun bir ölçüt olarak kullanılabilirliğini değerlendirilecektir.

Gereç ve Yöntemler: Kronik böbrek hastalığı olan 120 birey dahil edildi. Bireylerin sosyodemografik verileri, özgeçmişleri, kullandıkları tedaviler kaydedildi. Lipit düzeyleri, keratinin düzeyleri ve hesaplanmış glomerüler filtrasyon hızı (GFR) düzeyleri kaydedildi. Radyolojik görüntüleri incelendi. Framigham risk skorları hesaplandı. Veriler SPSS de analiz edildi, $p<0,05$ önemlilik ölçütü olarak alındı.

Bulgular: Bireylerin Framigham risk skorları değerlendirildiğinde 36'sı (%30) düşük, 52'si (%43,3) orta, 32'si (%26,7) yüksek olarak bulundu. GFR azaldıkça Framigham risk skoru daha yüksek saptandı.($X^2=36,78$ p=0,001*). Evre 5 kronik böbrek hastalığı renal replasman tedaviyle kardiyovasküler riskte düşme gözlenmedi. Lipit profile değerlendirildiğinde; yüksek yoğunluklu lipoprotein (HDL) düzeyleri framingham risk skorları ile daha korele şekilde evreye göre ters ilişkili bulundu. Koroner risk arttıkça HDL belirgin düzeyde düşük saptandı. Damar içi kalsifikasyonu olan bireylerde Framingham risk skoru daha yüksek saptandı. Skorun duyarlılığı kronik böbrek hastalığında kardiyovasküler riski göstermede yüksek bulundu. ($X^2=15,03$; P=0,001*)

Sonuç: Framingham risk skoru kronik böbrek hastalarında ateroskerozu ve kardiyovasküler riski belirlemede, kardioprotektif tedaviye karar vermekte özellikle invaziv yöntemleri kullanamadığımız hasta grubunda güvenilir bir araç olarak kullanılabilir.

Anahtar Kelimeler: *Kronik Böbrek Hastalığı; Framingham Risk Skoru; Kardiyovasküler Risk*

INTRODUCTION

Chronic kidney disease is a functional and structural abnormality that may cause impaired renal function for more than 3 months. Glomerular filtration rate is used in clinical practice to evaluate renal function. In the Kidney Disease Improving Global Outcome (KDIGO) classification, renal function is staged according to glomerular filtration rate (1).

Damage to almost all systems develops in chronic kidney disease. Especially cardiovascular system complications cause serious morbidity and mortality. Atherosclerosis is one of the most important factors that accelerate cardiac mortality in chronic kidney disease such as hypertension, cardiomyopathy, heart failure, ischemic heart disease, left ventricular hyperthyrophy, arrhythmias and uremic pericarditis (2). It is very difficult to visualize atherosclerosis in these patients. Radiographic agents facilitate the progression of existing renal disease with nephrotoxicity. Therefore, X-ray methods have been used to predict atherosclerosis and reliability studies have been performed (3,4).

Dyslipidemia develops as a result of increased triglycerides and decreased high density lipoprotein (HDL) in kidney damage (5,6). Statins are used to improve the lipid profile in patients. Statins lower total cholesterol and low density lipoprotein (LDL). While the decrease in lipids has a cardioprotective effect, the protective effect of antipidemic therapy in chronic kidney injury is unknown. However, cardiovascular risk is increased in chronic kidney disease and high LDL is known to cause an increase in coronary risk, so high LDL levels should be avoided in these patients. It should be aimed to keep LDL below 100 mg/dl. (7,8).

In dialysis treatment, the risk of cardiovascular disease is 500 times higher in individuals between 25-35 years of age, while this risk is 5 times higher in individuals over 85 years of age (9). In total, the risk of cardiovascular disease was found to be 15% higher in end-stage renal disease in all age groups compared to the general population. Cardiovascular diseases cause almost half of the deaths in stage 5 chronic kidney disease patients (10,11).

In our study, we aimed to evaluate the relationship between renal function and the risk of cardiovascular disease in patients with chronic kidney disease. At which stage the risk increases, how often cardiovascular follow-up should be performed according to the stages, whether cardiovascular risk changes with hemodialysis in end-stage renal failure and evaluation of prophylactic cardioprotective treatment, the place of treatment for lipid profile will be examined.

MATERIALS AND METHOD

Our study was approved by the Yozgat Bozok University Clinical Research Ethics Committee on 24.11.2022 with the protocol code 2017-KAEK-189_2022.11.24_01. Consent was obtained from individuals participating in the study. Based on the KDIGO definition, 120 individuals over the age of 18 with objective kidney damage and/or GFR below 60 ml/min/1.73 m² for at least 3 months were included in our study. Based on KDIGO chronic kidney disease staging, individuals with normal GFR but objective kidney damage were classified as Stage 1, individuals with GFR 60-89 ml/min/1.73 m² were classified as Stage 2, individuals with GFR 59-30 ml/min/1.73 m² were classified as Stage 3, individuals with GFR 29-15 ml/min/1.73 m² were classified as Stage 4, and individuals with GFR below 15 who had been on hemodialysis three times a week for at least 3 months were classified as Stage 5.

Estimad Glomerular Filtration Rate [EGFR(CKD-EPI) was used for glomerular filtration rate calculation. GFR (CKD-EPI) = 141 x minimum Serum creatinine/k.1 (Scr./k,1)a x maximum(Scr./k,1)-1.209 x 0.993Age] [x1.018 for women] [x1.159 for blacks]

[serum creatinine (mg/dl), k= 0.7 for women; 0.9 for men a= -0.329 for women; -0.411 for men min= serum creatinine /k min or 1; max = serum creatinine /k max or 1]

Personal information such as age, gender, race and smoking habits were recorded. After resting, blood pressure values were measured and recorded with the same sphygmomanometer placed on the brachial artery. Biochemical laboratory values such as fasting glucose, blood glucose, creatine, LDL, HDL, triglyceride values were recorded. Radiologic images of the patients for the last 6 months were analyzed.

For cardiologic risk assessment, Framigham Cardiovascular Risk Score was calculated based on gender, age, cholesterol levels, blood pressure and smoking. The calculation method was developed

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by Wilson (12). The resulting score indicates 10-year cardiovascular risk and was classified as low risk if below 10%, intermediate risk if between 10-20% and high risk if 20% or higher (13,14).

To evaluate aortic calcification, direct radiographs and computed tomography scans of the abdominal aorta taken within the last 6 months were reviewed. The presence of abdominal calcification reported by a radiologist was taken as basis. Direct radiographs of individuals without computarized tomography (CT) scans were evaluated by me. In order to test the accuracy, direct radiographs of individuals with computed tomography were also analyzed by us in the same blinded method and sensitivity calculation was performed.

Individuals with known coronary artery disease, individuals receiving lipid-lowering therapy, individuals with a body mass index of 30 or more, individuals with diabetes mellitus, individuals with a history of malignancy, individuals with proteinuria, pregnant women, and individuals with a low GFR of less than 3 months and individuals on hemodialysis for less than 3 months were excluded from the study.

Data were analyzed in statistical pacage for social sciences (SPSS) version 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0 Armonk, NY: IBM Corp). Descriptive measures were used for demographic data. Kolmogorov-Smirnov test was used to determine whether the data were normally distributed. Independent samples T-test was used to compare two groups for normally distributed data and nonparametric Mann-Whitney U Test was used for non-normally distributed data. Chi-Square test was used to compare the data. Statistically $p<0.05$ was accepted as significant.

RESULT

The study included 120 individuals with chronic kidney disease on routine hemodialysis program. Of the individuals, 67 (55.8%) were male and 63 (44.2%) were female. The minimum age was 21 years and the maximum age was 91 years; the mean age was 64.67±15.62 and the median age was 68 years. There was no statistical difference between the groups in terms of age and gender (Table.1).

Framigham risk score was found to be higher as renal function decreased ($P=0.001$; $p<0.05$ significant). While there was no statistically significant difference in LDL and HDL levels according to the stages of kidney disease, it was observed that comorbidity was the major factor in the high Framingham risk score. It was observed that the rate of calcification in the aorta increased rapidly as the glomerular filtration rate decreased, especially from stage 3 onwards. Although there was no difference between lipid levels, the increase in calcification was thought to be due to chronic kidney disease and diabetes mellitus causing deterioration in lipid morphology. Lipid levels are not sufficient to prevent atherosclerosis in these patients, but it is important to evaluate lipid morphology (Table 1).

When the framigham risk scores of the individuals were evaluated, 36 (30%) were low, 52 (43.3%) were moderate, and 32 (26.7%) were high. The mean LDL was 105.62 ± 42.37 and the mean HDL was 44.20± 10.23. However, as the Framingham risk score increased, HDL levels decreased. The reason for this inverse relationship is the normal HDL level in this patient group, which may be a protective factor (Table2).

Preferably non-contrast tomography and direct radiographs of the abdomen taken within the last 6 months; 97 individuals were evaluated by tomography and 23 individuals by direct radiography. In the evaluation of direct radiography and tomography, the direct radiographs of individuals with tomography were also examined and their reliability was tested. In 88 of 97 CT scans, calcification was found to be present on direct radiography. Sensitivity was above 90%. The relationship between the presence of intravascular calcification and Framingham risk score was statistically significant at $p = 0.001$ ($p<0.05$ significant). Intravascular calcification increased as Framingham risk score increased. Framingham risk score is a useful parameter in clinical practice to prevent the development of coronary complications in patients with chronic kidney disease (Table 2).

DISCUSSION

The fight against coronary artery disease, which is the most common cause of morbidity and mortality in chronic kidney disease, is very important. Invasive diagnostic and treatment methods such as non-

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Table 1. Evaluation of comorbidity, vascular calcification and framingham risk score according to Chronic Kidney Disease Stage

	Stage 1 CKD	Stage 2 CKD	Stage 3 CKD	Stage 4 CKD	Stage 5 CKD	Total (N)
N	8	10	28	28	46	120
Female/Male (n)	3/5	5/5	17/11	16/12	26/20	67/53
Diabetus Mellitus (n)	1	1	12	11	22	47
Hypertension (n)	3	7	23	27	44	104
LDL (mg/dl)	90.87 ± 38.92	113.30 ± 35.71	105.21 ± 50.97	105.82 ± 45.59	106.82 ± 45.59	105.62 ± 42.37
HDL (mg/dl)	46.87 ± 8.06	41.30 ± 9.16	46.35 ± 11.19	43.06 ± 9.32	43.76 ± 10.74	44.20 ± 10.23
Aortic calcification (n)	4	6	27	17	18	72
Framingham Risk Score	1.62± 6.41	2.90± 5.68	7.89± 4.88	10.03± 3.65	10.06± 3.96	
Framingham score Low/Medium/High (n) (x^2=36.78; P=0.001*)	6/2/0	9/0/1	11/10/7	5/14/9	5/26/15	36/52/32

CKD: Cronic renal disease; n: number of individuals; N: toatl number of individuals; LDL: Low density lipoprotein; HDL: Hight density lipoprotein; p <0.005*significant

Table 2. Distribution of factors affecting the level of Framingham Risk Score and vascular calcification

	Low risk	Medium risk	High risk	Total
n (%percent)	36 (%30)	52 (%43.3)	32 (%26.7)	120
Female/Male (n)	17/19	28/24	22/10	67/53
Diabetus Mellitus (n)	25	48	31	104
Hypertension (n)	3	19	25	47
LDL (mg/dl)	99.47± 41.17	113.50± 48.29	99.75± 30.94	105.62± 42.37
HDL (mg/dl)	47.16± 10.87	45.99± 9.79	37.96± 7.39	44.20± 10.23
Aortic calcification (n) % (percent) (x^2=15.03; P=0.001*)	n: 6 %16.7	n: 22 %42.3	n: 20 %62.5	n: 48 %40

n: number of individuals; N: toatl number of individuals; LDL: Low density lipoprotein; HDL: Hight density lipoprotein; p <0.005* significant

invasive evaluations such as ECG, echocardiography, biochemical markers or coronary angiography are used in the diagnosis of coronary artery diseases. However, it is very important to preserve the existing functions in individuals with renal failure. Contrast agents used during angiography cause nephropathy (15,16). Especially in patients with known renal failure, coronary artery disease is diagnosed by using non-invasive methods as much as possible and by considering the profit-loss relationship. Therefore, in our study, we aimed to see how valuable the Framingham risk score, which is one of the scoring systems used in the suspicion of coronary disease, is in determining cardiac risk and whether it can be a criterion for the initiation of cardioprotective treatment in patients with chronic kidney disease. In the study by Wilson et al., the effect of abdominal artery calcified deposits on the prediction of cardiovascular disease was examined in 2515 individuals and calcification deposits in the abdominal aortas of individuals were examined from abdominal radiographs. The sizes of the deposits were classified by comparing the vessel diameter and as a result, it was observed that vascular calcification was a marker of subclinical atherosclerosis and could be used as a marker in predicting cardiovascular disease (17). In the study by Meer et al. 6389 individuals were examined to investigate the severity of extracoronary atherosclerosis. The presence of abdominal atherosclerosis was checked by x-ray in individuals who had myocardial infarction and found to be significant. Abdominal artery calcification assessment as a non-invasive indicator of atherosclerosis is a significant criterion for the risk of myocardial infarction (18).

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The aim of the study by Okuno et al. was to evaluate whether abdominal aortic calcification is a reliable method in hemodialysis patients in addition to being reported as a marker of cardiovascular mortality in the community. A total of 515 hemodialysis patients with stage 5 kidney disease were included in the study. Abdominal lateral radiography was found to have prognostic significance as a cardiovascular indicator in hemodialysis patients (19). Similarly, in our study, Framingham risk score was found to be high in individuals with vascular calcification and the risk increased as the stage of renal disease progressed. Since the risk of cardiovascular disease increases as the stage progresses, precautions are necessary to reduce mortality, especially in stage 5 patients. In a study comparing hemodialysis and peritoneal dialysis, mortality due to cardiovascular diseases was found to be higher during hemodialysis (20). In our study, all of our patients in the group with stage 5 chronic kidney disease received hemodialysis treatment and peritoneal dialysis may be recommended in individuals with high Framingham risk score in order to reduce cardiac mortality during dialysis if there is no contraindication for peritoneal dialysis (21). In addition, there is a need to evaluate peritoneal dialysis patients with Framingham risk score to determine whether it is protective in terms of cardiac risk compared to hemodialysis in the long term. Likewise, there is a need for a study on whether cardiac mortality decreases with renal transplantation, another renal replacement therapy. Although most of the medical treatments used in diseases are used with renal dosing, most of the drug doses in individuals with coronary disease are used without dose adjustment according to chronic kidney disease. The main reason for this is that even if renal function is impaired in this group, these individuals have a higher cardiac risk than other patient groups. However, drug levels may decrease with dialysis in dialysis patients. This may cause mortality to be higher in stage 5 chronic kidney disease. Therefore, higher doses of cardioprotective therapies may be required in hemodialysis patients. For this, blood levels of the most commonly used drugs in clinical practice should be evaluated (22,23). There is a lot of literature data on lipid levels and risk factors for coronary artery disease. In addition to lipid levels, genetic morphisms are also examined. Studies on oxidelipoprotein receptors have provided data proving the effect of lipids on the vascular structure (24,25). However, it is almost impossible to evaluate these in clinical practice. For this reason, lipid parameters routinely used in clinical formulations are included. In this patient group, it is not HDL level but LDL that affects the score; on the contrary, HDL may be cardioprotective in these patients. It is important to predict cardiovascular risk with non-invasive methods in kidney disease. In patients with chronic kidney disease, the risk of cardiovascular disease increases as GFR decreases. As the stage increased, the Framingham risk score was found to be higher. No reduction in cardiovascular risk was observed with hemodialysis in stage 5 patients. Studies are needed in other renal replacement therapies. HDL has a cardioprotective effect in patients with chronic kidney disease and isolated LDL-lowering therapies should be used.

CONCLUSION

In conclusion, Framingham risk score is a reliable tool for predicting atherosclerosis and cardiovascular disease risk in patients with chronic kidney disease.

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The authors declare that they have no conflict of interest to disclose

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