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Is the magnesium phosphate ratio a predictor of arrhythmia in patients undergoing hemodialysis?

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ABSTRACT

Aim: Sudden death due to coronary artery disease, heart failure, arrhythmia or hyperkalemia constitutes the majority of cardiovascular causes in patients with end-stage renal disease. Magnesium plays an important role in many processes that regulate cardiovascular functions such as endothelial function, regulation of vascular tone and myocardial excitability. In addition, hyperphosphatemia is very common in patients with end-stage renal disease and is associated with an increased risk of mortality in hemodialysis patients. Our aim in this study; to determine the role of Mg/PO_4 ratio in predicting arrhythmia in patients with end-stage renal disease receiving hemodialysis.

Material and Method: A total of 103 consecutive patients admitted to the cardiology outpatient clinic and receiving hemodialysis for chronic renal failure were included in the study. Between January 2018 and October 2022, patients monitored with 24-hour rhythm holter ECG were recruited. Patients were analyzed by dividing into 2 groups as those with arrhythmia detected in 24-hour rhythm Holter ECG (group 1: 51 patients) and those without (group 2: 52 patients).

Result: The mean age of the patients in the study was significantly higher in group 1 compared to group 2 (66.96±10.27 and 62.21±10.50, p=0.02, respectively). When the 24-hour rhythm Holter ECGs of the patients were examined, the most common arrhythmia was ventricular extrasystole with a rate of 18.4% (n=19), and paroxysmal AF was the second with a rate of 9.7% (n=10). In the univariate regression analysis we performed for arrhythmia predictivity in patients receiving hemodialysis; age (OR: 1.046; 95%CI: 1.005-1.088, p=0.02), LVEF (OR: 0.941; 95%CI: 0.895-0.989, p=0.01), mid-severe MR (OR: 0.553; 95%CI: 0.215-1.424, p=0.22), Na (OR: 1.119; 95%CI: 0.967-1.294, p=0.13), Hemoglobin (OR: 0.872; 95%CI: 0.710-1.069, p=0.18), total cholesterol (OR: 1.006; 95%CI: 0.997-1.016, p=0.19), LDL (OR: 1.012; 95%CI: 0.998-1.026, p=0.10), Mg (OR: 0.117; 95%CI: 0.015- 0.941, p=0.04), PO_4 (OR: 1.664; 95%CI: 1.093-2.532, p=0.01), Mg/PO_4 ratio (OR: 0.002; 95%CI: 0.000-0.104, p=0.002) detected as arrhythmia predictors. In the multivariate regression analysis, independent predictors for the presence of arrhythmia were determined using 2 different models. In the model 1; age (OR: 0.993; 95%CI: 0.956 1.031, p=0.70), LVEF (OR: 0.955; 95%CI: 0.916-0.994, p=0.026), Mg (OR: 0.136; 95%CI: 0.014-1.308), p=0.08), PO_4 (OR: 1.545; 95%CI: 0.989- 2.414, p=0.056) (Table 6). In the model 2; age (OR: 0.988; 95%CI: 0.951-1.026, p=52), LVEF (OR: 0.955; 95%CI: 0.917-0.995, p=0.029), Mg/PO_4 ratio (OR: 0.002, 95%CI: 0.000-0.101 p=0.002) was detected independent predictors for the presence of arrhythmia. ROC analysis (Figure) showed that LVEF<54.5%, with 64% sensitivity and 53% specificity ([AUC]: 0.666, 95% CI: 0.560-0.772, p=0.004), Mg/PO_4 ratio<0.45, with 64% sensitivity and 65% specificity ([AUC]: 0.674, 95% CI: 0.570-0.778, p=0.002), predicts arrhythmia in hemodialysis patients

Conclusion: In our study, it was concluded that the Mg/P ratio, which can be calculated simply, is a predictor of arrhythmia in hemodialysis patients.

Keywords: Arrhythmia, hemodialysis, predictivity, Holter ECG

INTRODUCTION

According to the USA Renal Data System Report (1), the number of patients undergoing hemodialysis due to serious chronic renal failure tends to increase significantly. Despite the increasing technology and experience in hemodialysis (HD), the risk of death still remains high. Five-year life expectancy is 35% in the USA and 60% in Japan, lower than in the general population (2,3). Cardiovascular disease are the cause of death in approximately 40% of patients receiving hemodialysis (4). This situation may not be explained only by cardiovascular (CV) risk factors, but also by non-traditional risk factors such as inflammation, oxidative stress, anemia and uremia (5). Sudden death from coronary artery disease (CAD), heart failure, or arrhythmia for the majority of CV causes in patients with ESRD (6).

The most important factors for arrhythmia in chronic renal failure patients entering HD are; left ventricular dysfunction, disturbance of electrolyte values such as potassium and magnesium (Mg), hypertension, diabetes mellitus (DM), presence of CAD. Many studies have investigated the effects of these factors on arrhythmia, but their relative importance is not fully known (7). Mg and phosphate (PO_4) minerals, which are electrolytes in the blood, are important minerals in the pathophysiology

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of atherogenesis. Mg plays an important role in many processes that regulate CV functions such as endothelial function, regulation of vascular tone and myocardial excitability (8,9). In the general population, a lower serum Mg level and/or lower dietary Mg intake is associated with an increased incidence of hypertension, Type 2 DM, metabolic syndrome, cerebrovascular disease, myocardial infarction, atrial fibrillation, and sudden cardiac death (10-12).

However, high serum PO_4 concentration, even within the normal range, has been reported to be predictive of the development of atherosclerosis and mortality in patients with normal renal function (13,14). Hyperphosphatemia is very common in patients with end-stage renal disease and is associated with an increased risk of mortality in hemodialysis patients. Patients in the high PO_4 group also had a non-significantly increased relative risk of death from other causes of cardiac and cerebrovascular death (14). Our aim in this study; to determine the role of Mg/PO_4 ratio in predicting arrhythmia in patients with end-stage renal disease receiving hemodialysis.

MATERIAL VE METHOD

Our study was designed as retrospective, observational. The study was initiated with the approval of the Bakırçay University Non-Invasive Clinical Researches Ethics Committee (Date: 2022, Decision No: 770). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

A total of 103 consecutive patients admitted to the cardiology outpatient clinic and receiving hemodialysis for chronic renal failure were included in the study. Between January 2018 and October 2022, patients monitored with 24-hour rhythm holter ECG were recruited.

Patients whose baseline ECG is not in sinus rhythm and known arrhythmia, younger than 18 years of age, and had malignancy, active infection, prosthetic valve disease, cardiac pacing, and whose transthoracic echocardiographic (TTE) measurements and 24-hours rhythm Holter ECG cannot be optimized were excluded from the study. In addition, diseases that may cause an arrhythmogenic condition such as amyloidosis and Fabry disease were excluded from the study. The results of blood tests, ECG and TTE findings, and 24- hours rhythm Holter ECG results were obtained from hospital records. The blood analysis results of these patients include the values after hemodialysis, and Holter ECG has been performed at least 1 day after receiving hemodialysis.

Patients were analyzed by dividing into 2 groups as those with arrhythmia detected in 24-hour rhythm Holter ECG (group 1: 51 patients) and those without (group 2: 52 patients).

Arrhythmia Definition in Rhythm Holter ECG

Non-sustained ventricular tachycardia (NSVT) was defined as ventricular-derived tachycardia with a wide QRS complex lasting more than 3 consecutive beats and lasting less than 30 seconds. Supraventricular tachycardia was defined as atrial origin tachycardia with narrow QRS complex and regular RR distance. Paroxysmal AF (Atrial Fibrillation) was defined as atrial origin tachycardia attack with narrow QRS complex and irregular RR distance in rhythm holter ECG. MAT (Multifocal Atrial Tachycardia) was defined as 3 or more different P waves in rhythm Holter ECG, variable P-P, P-R, R-R intervals and atrial origin tachycardia (atrial rhythm 100-180/min) attack.

Statistical Analysis

Analysis was done using IBM SPSS Statistics 24.0 program. The normality distribution of numerical variables was determined by the Kolmogorov-Smirnov test. Numerical variables were noted as mean and standard deviation using the independent Student's t test if they were normally distributed. Numerical variables were noted as IQR (Q (25-75)) using the mann whitney u test if they were not normally distributed. Chi-square and Fisher's exact tests were used to compare categorical variables and reported as number (n) and percentage (%). Logistic regression analysis was performed for the predictiveness of arrhythmia and statistical process was completed with ROC curve analysis. P values below 0.05 were considered statistically significant.

The number of individuals to be included in the study was made using the G*Power 3.1.9.7 program. Estimated sample size was calculated using an independent two-sample-t test, with 80% power, α=0.05 error level, and Cohen (d) effect size "medium"=0.5. Accordingly, it was found appropriate to complete the study with at least 102 patients. In the post hoc analysis the power (1-β err probe) was determined as 0.809 with alpha 0.05 error level, Cohen (d) effect size=0.5.

RESULTS

The mean age of the patients in the study was significantly higher in group 1 compared to group 2 (66.96±10.27 and 62.21±10.50, p=0.02, respectively). The most common comorbid conditions in the patients were hypertension and coronary artery disease, but there was no significant difference between the two groups (hypertension 49% in group 1 and 46% in group 2, p=0.77, coronary artery disease 39% in group 1 and 35% in group 2, p=0.62). When the gender was compared, the number of male patients was higher, but no statistically significant difference was found (Group 1: 61% and group 2: 50%, p=0.27). The baseline clinical features and comorbid conditions of the patients are shown in **Table 1**.

Table 1. Comorbid conditions and baseline clinical features of patients

Variables, n (%)	Group 1 (n=51)	Group 2 (n=52)	p
Age, year	66.96±10.27	62.21±10.50	0.02
Male sex	31 (61)	26 (50)	0.27
Hypertension	25 (49)	24 (46)	0.77
Diyabetes mellitus	14 (27)	14 (27)	0.952
Coronary artery disease	20 (39)	18 (35)	0.62
Hyperlipidemia	12 (24)	15 (29)	0.54
Peripheral artery disease	4 (7.8)	4 (7.7)	0.977
Thyroid disease	8 (16)	6 (12)	0.53
Pulmonary embolism history	3 (5.8)	3 (5.9)	0.652
Anemia	16 (31)	9 (17)	0.096
Chronic pulmonary disease	6 (11.8)	4 (7.7)	0.35
Smoking	16 (31)	13 (25)	0.47
Alcohol use	3 (5.9)	5 (9.6)	0.36
Hemodialysis time, hour	3.1±0.34	3.2±0.27	0.68

n: number of patients, Group 1: those with arrhythmia, Group 2: those without arrhythmia.

When the 24-hour rhythm Holter ECGs of the patients were examined, the most common arrhythmia was ventricular extrasystole with a rate of 18.4% (n=19), while paroxysmal AF was the second with a rate of 9.7% (n=10). Other arrhythmia types and rates are summarized in **Table 2**.

Table 2. Arrhythmias detected in rhythm Holter ECG inm hemodialysis patients

Arrhythmia type, n (%)	Hemodialysis patients (n=103)
Ventricular extrasystole	19 (18.4)
Paroxysmal AF	10 (9.7)
Supraventricular extrasystole	6 (5.8)
Supraventricular tachycardia	6 (5.8)
Atrial tachycardia	5 (4.9)
Non sustained VT	3 (2.9)
Multifocal atrial tachycardia	2 (1.9)

n: number of patient, AF: atrial fibrillation, VT: ventricular tachycardia

There was no statistical difference between the two groups in terms of body mass index (BMI), systolic blood pressure (sBP) and pulse rate (BMI; 23.80 (22.2-27.3) and 23.45 (21.87-28.25), p= 0.85, sBP; 140 (120-151) and 140 (127-159), p =0.48, heart rate; 83.05±15.79 and 82.98±14.41, p= 0.97, group 1 and 2, respectively). Among the transthoracic echocardiographic findings, LVEF (left ventricular ejection fraction) value was found to be significantly lower in group 1 than group 2 (50.00±8.92 and 54.42±8.48, p=0.01, respectively). When the blood analyzes of these patients were examined, the Mg, P and Mg/PO_4 ratios showed significant differences between the two groups (Mg; 1.92 (1.85-2.01) mmol/L and 2.01 (1.91-2.17), p=0.02, PO_4; 4.58 (4.1-5.18) mmol/L and 3.9 (3.6-4.87), p=0.003, Mg/PO_4 ratio; 0.43 (0.36-0.50) and 0.51 (0.41-0.61), p=0.002, group 1 and 2, respectively).

In **Table 3**, imaging, examination findings and blood analysis results of the patients are given in detail. The drugs they currently use are presented in **Table 4**.

Table 3. Imaging, examination findings and blood analysis results of patients

Variables	Group 1 (n=51)	Group 2 (n=52)	p
Body mass index, kg/m²	23.80 (22.2-27.3)	23.45 (21.87-28.25)	0.85
Pulse, beat/min	83.05±15.79	82.98±14.41	0.97
Systolic BP, mmHg	140 (120-151)	140 (127-159)	0.48
Diastolic BP, mmHg	80 (70-91)	80 (70-90)	0.87
LVEF, %	50.00±8.92	54.42±8.48	0.01
Mid-severe MR, n (%)	14 (27)	9 (17)	0.21
Mid-severe MS, n (%)	4 (7)	6 (11)	0.38
Mid-severe AR, n (%)	6 (11)	5 (10)	0.72
Mid-severe AS, n (%)	7 (14)	12 (23)	0.22
Mid-severe TR, n (%)	13 (25)	12 (23)	0.77
Fasting blood glucose, mg/dL	101 (93-123)	96 (88-119)	0.11
Urea, mg/dL	23.8 (12.3-32.1)	15.4 (11.77-34.92)	0.74
Creatinine, mg/dL	2.82 (2.14-3.7)	2.73 (1.91-2.99)	0.35
Na, mmol/L	139 (137-140.5)	138 (137-140)	0.12
K, mmol/L	4.33 (4.04-5.1)	4.38 (4-4.9)	0.49
Ca, mmol/L	8.39±0.77	8.44±0.64	0.68
Mg, mmol/L	1.92 (1.85-2.01)	2.01 (1.91-2.17)	0.02
PO_4, mmol/L	4.58 (4.1-5.18)	3.9 (3.6-4.87)	0.003
Mg/PO_4 oranı	0.43 (0.36-0.50)	0.51 (0.41-0.61)	0.002
Leukocyte, /mm³	8.8 (7.82-10.65)	8.91 (8.1-10.59)	0.76
Hemoglobin, g/dL	12.16±2.01	12.66±1.84	0.18
Thrombocyte, /mm³	244 (211-264)	239.5 (208-296)	0.68
TSH, mIU/L	1.38 (0.84-1.92)	1.52 (0.88-2.16)	0.55
B12 vitamin, pg/mL	211.4 (191-266)	220 (189-308)	0.73
Ferritin, ng/mL	41.53 (31.3-62)	45 (39.3-54.9)	0.46
Total cholesterole, mg/dL	211.37±41.76	198.92±46.76	0.19
Trygliseride, mg/dL	184±85.65	176±81.75	0.65
HDL-C, mg/dL	41.26±9.85	40.76±10.85	0.82
LDL-C, mg/dL	127.64±30.51	116.31±32.49	0.09
CRP, mg/dL	3.28±0.76	3.31±0.61	0.72

n: number of patient, BP: blood pressure, LVEF: left ventriclel ejection fraction, MR: mitral regurgitation, MS: mitral stenoz, AR: aort regurgitation, AS: aort stenoz, TR: tricuspit regurgitation, Na: sodium, K: potassium, Ca: calsium, Mg: magnesium, PO_4: phosphate, TSH: thyroid stimulant hormone, HDL-C: high density lipoprotein-cholesterole, LDL-C:low density lipoprotein-cholesterole, Grup 1: those with arrhythmia, Grup 2: those without arrhythmia. Those with normal distribution of continuous variables were presented as the mean±SD by using the Student's t test. Continuous variables that did not show normal distribution were presented as IQR (25-75) by applying the Mann Whitney U test.

Table 4. Medications of patients

Drugs, n (%)	Group 1 (n=51)	Group 2 (n=52)	p
Betablocker	18 (35)	11 (21)	0.11
Ca channel blocker (Dhp)	12 (24)	13 (25)	0.86
Ca channel blocker (Non-dhp)	7 (14)	7 (13)	0.96
Acetylsalicylic acid	18 (35)	16 (31)	0.62
Insulin	5 (10)	5 (10)	0.97
Statin	12 (24)	11 (21)	0.77
Oral iron preparation	9 (18)	9 (17)	0.96
Oral B12 vitamini	6 (12)	8 (15)	0.59

n: number of patient, Ca: calsium, Dhp: dihydropyridine, Group 1: those with arrhythmia, Group 2: those without arrhythmia.

In the univariate regression analysis we performed for arrhythmia predictivity in patients receiving hemodialysis; age (OR: 1.046; 95%CI: 1.005-1.088, p=0.02), LVEF (OR: 0.941; 95%CI: 0.895-0.989, p=0.01), mid-severe MR (OR: 0.553; 95%CI: 0.215-1.424, p=0.22), Na (OR: 1.119; 95%CI: 0.967-1.294, p=0.13), Hemoglobin (OR: 0.872; 95%CI: 0.710-1.069, p=0.18), total cholesterol (OR: 1.006; 95%CI: 0.997-1.016, p=0.19), LDL (OR: 1.012; 95%CI: 0.998-1.026, p=0.10), Mg (OR: 0.117; 95%CI: 0.015- 0.941, p=0.04), PO_4 (OR: 1.664; 95%CI: 1.093-2.532, p=0.01), Mg/PO_4 ratio (OR: 0.002; 95%CI: 0.000-0.104, p=0.002) detected as arrhythmia predictors. In the multivariate regression analysis, independent predictors for the presence of arrhythmia were determined using 2 different models. In the model 1; age (OR: 0.993; 95%CI: 0.956 1.031, p=0.70), LVEF (OR: 0.955; 95%CI: 0.916-0.994, p=0.026), Mg (OR: 0.136; 95%CI: 0.014-1.308), p=0.08), PO_4 (OR: 1.545; 95%CI: 0.989- 2.414, p=0.056). In the model 2; age (OR: 0.988; 95%CI: 0.951-1.026, p=52), LVEF (OR: 0.955; 95%CI: 0.917-0.995, p=0.029), Mg/PO_4 ratio (OR: 0.002, 95%CI: 0.000-0.101 p=0.002) was detected independent predictors for the presence of arrhythmia. Logistic regression analysis is shown in **Table 5**. ROC analysis (**Figure**) showed that LVEF<54.5%, with 64% sensitivity and 53% specificity ([AUC]: 0.666, 95% CI: 0.560-0.772, p=0.004), Mg/PO_4 ratio<0.45, with 64% sensitivity and 65% specificity ([AUC]: 0.674, 95% CI: 0.570-0.778, p=0.002), predicts arrhythmia in hemodialysis patients.

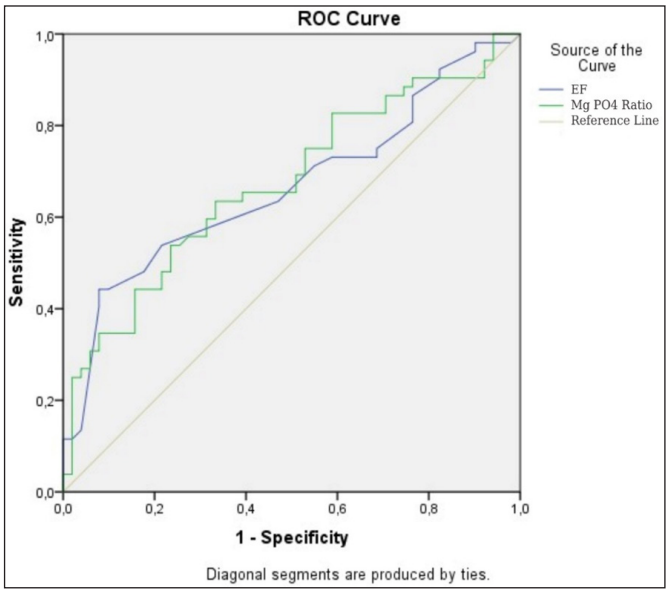

Figure. Receiver Operating Characteristic curve analysis for arrhythmia predictivity in hemodialysis patients.

DISCUSSION

The important finding of this study is that the Mg/PO_4 ratio determined by low magnesium and high phosphate values is a predictor of arrhythmia in patients receiving hemodialysis for chronic renal failure. After multivariate regression analysis, lower magnesium phosphate ratio and lower LVEF were potential risk factors.

Lu Wei et al. (15) found low serum Mg concentration to be a predictive factor of major adverse cardiac and cerebrovascular events (MACCE) in 290 hemodialysis patients. In the management of hemodialysis patients, it has been stated that a Mg level lower than 1.04 mmol/L can predict especially cardiovascular mortality.

Table 5. Logistic regression analysis for arrhythmia predictive in hemodialysis patients

Variables	Univarite Logistic Regression			Multivariate Logistic Regression Model 1			Multivariate Logistic Regression Model 2		
	OR	95 % CI	p	OR	95 % CI	p	OR	95 % CI	p
Age	1.046	1.005-1.088	0.02	0.993	0.956-1.031	0.7	0.988	0.951-1.026	0.52
LVEF	0.941	0.895-0.989	0.01	0.955	0.916-0.994	0.026	0.955	0.917-0.995	0.029
Mid-Severe MR	0.553	0.215-1.424	0.22						
Na	1.119	0.967-1.294	0.13						
Hemoglobin	0.872	0.710-1.069	0.18						
T. cholesterol	1.006	0.997-1.016	0.19						
LDL	1.012	0.998-1.026	0.10						
Mg	0.117	0.015-0.941	0.04	0.136	0.014-1.308	0.08			
PO_4	1.664	1.093-2.532	0.01	1.545	0.989-2.414	0.056			
Mg/PO_4 ratio	0.002	0.000-0.104	0.002				0.002	0.000-0.101	0.002

OR: odds ratio, CI: confidence interval, LVEF: left ventricular ejection fraction, MR: mitral regurgitation, Na: sodium, LDL: low density lipoprotein, Mg: magnesium, PO_4: phosphate.

Magnesium is the most abundant ion in our body. A wide range of effects may occur with low Mg, ranging from vascular calcification, coronary artery calcification, and abdominal vascular calcification (16-18) to asthma development, a predisposing effect to chronic inflammation, myocardial remodeling, and electrophysiological abnormalities (19,20). In recent studies (21-23), higher Mg levels were associated with less arrhythmia and cardiovascular death after and during dialysis. In our current study, the Mg level was found to be significantly lower in the arrhythmia group.

In a study which data from two national randomized samples of hemodialysis patients (n=12,833) were used to test the hypothesis that high serum PO_4 contributes to the major causes of cardiac death, death from CAD, sudden death, infection and death from unknown causes were found to be higher in the high PO_4 group (>6.5 mg/day) than the lower PO_4 group (<6.5 mg/dl). This study (14) identifies strong associations between elevated serum PO_4 and causes of cardiac death in HD patients, particularly deaths from CAD and sudden death. More effective treatment measures to reduce the prevalence of these factors in HD patients may result in improved survival.

In previous studies (24,25), the relationship between coronary ischemia and endothelial functions and Mg/PO_4 ratio was investigated. The predisposition of magnesium and phosphate to thrombosis through atherosclerosis and inflammation is known. The association between low Mg levels and increased cardiac mortality has been noted by several investigators. Chipperfield et al. (26) found low myocardial Mg levels in cases of sudden cardiac death. Electrophysiological changes, albeit minimal, were recorded with Mg replacement and an antiarrhythmic effect was observed (27,28). Schwartz et al. (29) found a negative correlation between cardiac arrhythmia and phosphate level in early stage sepsis. Since both Mg and PO_4 can affect cardiac arrhythmia to a certain extent, we can think that their ratio to each other is also effective. In this study, we aimed to reveal the potential effect of Mg/PO_4 ratio on the development of arrhythmia.

The frequency of arrhythmias in patients undergoing hemodialysis is too high to be underestimated. In a study of 160 patients with end-stage renal disease receiving hemodialysis, 92% of arrhythmic events were detected. The frequency of these arrhythmias was mostly ventricular events with 81%, followed by supraventricular events with 51% (30). Similar to previous studies by Sforzini et al. (31), the most common arrhythmia in our study was ventricular events (37% among all arrhythmias).

The management of morbidity and mortality due to arrhythmia in dialysis patients is still difficult and opportunities to turn this situation in their favor are limited. Our most important diagnostic tool that facilitates this situation is ECG monitoring. In particular, it is possible to detect atrial fibrillation (paroxysmal), which we have identified as the cause of cerebrovascular disease with severe consequences, with 24-hour rhythm Holter ECG without creating both material and moral burden (32). Atrial fibrillation becomes chronic; it has adverse effects such as stroke, heart failure, and decreased LV systolic functions due to tachycardiomyopathy. Based on this, both a decrease in LVEF triggers atrial fibrillation and the development of atrial fibrillation enters a vicious circle with worsening LVEF (33). The DEFINITE (Significance of follow-up left ventricular ejection fraction measurements in the Defibrillators in Non-Ischemic Cardiomyopathy Treatment Evaluation trial) study (34) showed that mortality tends to decrease and the probability of experiencing arrhythmic events decreases in the group with left ventricular recovery. For this reason, it is expected that the frequency of ventricular arrhythmias will increase as the left ventricular EF value decreases in patients with ischemic or non-ischemic heart failure. In our current study, LVEF was lower in the group with arrhythmia.

Study Limitations

Our study has a few limitations, except that it is single-center and retrospective. Although the Holter ECG records of the patients were at least 24 hours after hemodialysis, we did not have access to the duration of the dialysis procedure, hemodynamic variables and fluid-electrolyte balance findings. Based on the assumption that the expected frequency of arrhythmias is higher in hemodialysis patients, it may be important to obtain rhythm recordings longer than 24 hours.

CONCLUSION

The Mg/PO_4 ratio, which can be calculated simply, is a predictor of arrhythmia in hemodialysis patients. It can be thought that our study can be a pioneer in this regard, supported by future multicenter and prospective studies..

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bakırçay University Non-Invasive Clinical Research Ethics Committee (Date: 2022, Decision No: 770).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The author has no conflicts of interest to declare.

Financial Disclosure: The author declares that this study has received no financial support.

Author Contributions: The author declares that he has participated in the design, execution, and analysis of the paper, and he has approved the final version.

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