The prevalence and predictors of atrial fibrillation in hemodialysis patients

Hemodiyaliz hastalarında atriyal fibrilasyon sıklığı ve belirleyicileri

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Objectives: The aim of this study was to determine the prevalence of atrial fibrillation in long-term hemodialysis patients and to identify clinical and echocardiographic risk factors.

Study design: The study included 183 patients (93 males, 90 females; mean age 52±17 years) who had been on long-term hemodialysis treatment (mean 41.6±39.8 months) and had preserved systolic function. Atrial fibrillation was determined electrocardiographically and the patients were divided into two groups depending on the presence or absence of atrial fibrillation. Conventional and tissue Doppler echocardiographic examinations were performed on interdialytic days. Clinical, laboratory, and echocardiographic parameters were compared.

Results: Twenty-four patients (13.1%) had atrial fibrillation. Patients with atrial fibrillation significantly differed in terms of higher age (64.9±9.8 *vs.* 49.9±16.6 years; p<0.001), higher frequency of coronary artery disease (37.5% *vs.* 10.7%; p=0.008), and lower serum albumin level (3.6±0.4 *vs.* 3.9±0.5 mg/dl; p=0.015). Echocardiographic examination showed significantly increased left and right atrial diameters (p<0.05), higher incidence of mitral and/or aortic calcification (p=0.033), increased systolic pulmonary artery pressure (38.1±6.1 *vs.* 28.5±5.5 mmHg, p<0.001) and E/E' ratio (11.8±3.8 *vs.* 8.8±4.7, p=0.008) in patients with atrial fibrillation. In multivariate logistic regression analysis, age (OR 1.09; 95% CI 1.00-1.17; p=0.036) and right atrial diameter (OR 1.19; 95% CI 1.05-1.35; p=0.008) were independent risk factors for the development of atrial fibrillation.

Conclusion: Our findings highlight age and right atrial diameter as independent predictors of atrial fibrillation in hemodialysis patients. In addition, the E/E' ratio and pulmonary artery pressure may be considered new risk factors of atrial fibrillation in this population.

Key words: Atrial fibrillation/etiology; echocardiography; kidney failure, chronic/complications; renal dialysis/adverse effects.

Amaç: Bu çalışmada uzun dönem hemodiyaliz tedavisi gören hastalarda atriyal fibrilasyon sıklığı araştırıldı ve atriyal fibrilasyon için klinik ve ekokardiyografik risk faktörlerinin belirlenmesi amaçlandı.

Çalışma planı: Çalışmaya sistolik fonksiyonları bozulmamış olan ve uzun dönemdir (ort. 41.6±39.8 ay) hemodiyaliz tedavisi gören 183 hasta (93 erkek, 90 kadın; ort. yaş 52±17) alındı. Atriyal fibrilasyon varlığı elektrokardiyografi ile belirlendi ve hastalar atriyal fibrilasyon olup olmamasına göre iki gruba ayrıldı. Diyaliz uygulanmayan günlerde konvansiyonel ve doku Doppler ekokardiyografik inceleme yapıldı. İki grup klinik, laboratuvar ve ekokardiyografik veriler açısından karşılaştırıldı.

Bulgular: Yirmi dört hastada (%13.1) atriyal fibrilasyon saptandı. Atriyal fibrilasyonlu hastalar yüksek yaş (64.9±9.8 ve 49.9±16.6; p<0.001), yüksek koroner arter hastalığı sıklığı (%37.5 ve %10.7; p=0.008) ve düşük serum albümin düzeyi (3.6±0.4 ve 3.9±0.5 mgr/dl; p=0.015) açısından anlamlı farklılık gösterdi. Bu grupta ekokardiyografik verilerden sol ve sağ atriyum çapları (p<0.05), mitral ve/veya aortik kalsifikasyon sıklığı (p=0.033), sistolik pulmoner arter basıncı (38.1±6.1 ve 28.5±5.5 mmHg, p<0.001) ve E/E' oranı (11.8±3.8 ve 8.8±4.7, p=0.008) anlamlı derecede artmış bulundu. Çokdeğişkenli lojistik regresyon analizinde, yaş (odds oranı 1.09; %95 GA 1.00-1.17; p=0.036) ve sağ atriyum çapının (odds oranı 1.19; %95 GA 1.05-1.35; p=0.008) atriyal fibrilasyon gelişimi için bağımsız etkenler olduğu görüldü.

Sonuç: Bulgularımız hemodiyaliz hastalarında yaş ve sağ atriyum çapını atriyal fibrilasyon gelişimi için bağımsız öngördürücü olarak öne çıkardı. Ayrıca, E/E' oranı ve pulmoner arter basıncı bu hasta grubunda atriyal fibrilasyon gelişimi için yeni risk faktörleri olarak değerlendirilebilir.

Anahtar sözcükler: Atriyal fibrilasyon/etyoloji; ekokardiyografi; böbrek yetersizliği, kronik; böbrek diyalizi/yan etki.

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Cardiovascular diseases are among the leading causes of morbidity and mortality in hemodialysis patients.[1] Atrial fibrillation is the most common type of sustained cardiac arrhythmia and it is associated with increased mortality and thromboembolic risk in hemodialysis patients.[2,3] In addition, the frequency of atrial fibrillation is increased in chronic hemodialysis patients.[4-11] Atrial fibrillation with rapid ventricular response may cause adverse events, such as angina pectoris, hypotension, congestive heart failure, and increased risk for thromboembolism. Hence, the presence of concomitant atrial fibrillation is of special importance in these patients.[12]

Several studies have been performed to determine the clinical and echocardiographic predictors of atrial fibrillation in hemodialysis patients, and many risk factors have been defined.[3-9] Additionally, pulmonary hypertension and diastolic dysfunction are predisposing factors for the development of atrial fibrillation in the general population.[13] The ratio of early diastolic mitral inflow velocity to diastolic mitral annular velocity (E/E') is a noninvasive marker of diastolic filling pressure.[14] It has also been demonstrated that this index is a useful parameter for predicting the risk for atrial fibrillation in patients with acute anterior myocardial infarction[15] and hypertensive patients.[16] However, the association between atrial fibrillation, E/E', and pulmonary artery pressure has not been investigated in hemodialysis patients.

The aim of the present study was to determine the prevalence of atrial fibrillation in long-term hemodialysis patients and to identify clinical and echocardiographic risk factors.

PATIENTS AND METHODS

Study population. A total of 183 patients (93 males, 90 females; mean age 52±17 years) were enrolled in this study, who had been on maintenance hemodialysis for at least three months at our institution between January and March 2008. The mean duration of hemodialysis was 41.6±39.8 months. Patients with moderate-to-severe valvular heart disease were excluded. The study protocol was approved by the local ethics committee, and all patients were informed about the study protocol, and informed consent was obtained from each participant. All patients underwent a detailed medical history taking, physical examination, routine laboratory tests, and 12-lead surface electrocardiography.

Atrial fibrillation was determined electrocardiographically and the patients were divided into two groups depending on the presence (group I) or absence (group II) of atrial fibrillation. Atrial fibrillation that terminated spontaneously and/or lasted for seven days or less was classified as paroxysmal; if it lasted for more than seven days or terminated with pharmacological therapy or direct-current cardioversion, it was classified as persistent; when cardioversion failed or was not attempted, it was classified as permanent.[13]

Patients with a previous history of acute myocardial infarction, angioplasty, or coronary bypass graft were considered to have coronary artery disease. Hypertension was diagnosed according to the criteria defined by the European Society of Hypertension and European Society of Cardiology.[17] Diabetes mellitus was diagnosed according to the criteria defined by the American Diabetes Association.[18]

Echocardiographic evaluation. Echocardiographic examinations were performed using a Vivid 7 device with a 2-4 MHz phased array transducer (General Electric, Horten, Norway) on interdialytic days by the same cardiologist. Standard M-mode, two-dimensional, and color Doppler imaging were performed in the parasternal and apical views. Representative values were obtained from the averages of three measurements. End-diastole was defined as the frame with the largest cavity area immediately before the onset of QRS, and end-systole as the frame with the smallest cavity area. Left ventricular (LV) end-diastolic volume, LV end-systolic volume, and LV ejection fraction were calculated from two-dimensional recordings using the modified biplane Simpson's method. Left ventricular mass was calculated with the Devereux formula[19] and was indexed to body surface area. Early mitral inflow velocity (E, cm/sec) was measured using the pulsed-wave Doppler method by placing the sample volume at the level of the mitral valve leaflet tips. Tissue Doppler-derived diastolic mitral annular velocity (E', cm/sec) was measured from the lateral corner of the mitral annulus in the apical four-chamber view. The E/E' ratio, an important noninvasive marker of LV filling pressure, was calculated.[14] Systolic pulmonary artery pressure was calculated using the modified Bernoulli equation.[20] Patients with calcification of the mitral or aortic valves were also noted.

The clinical and echocardiographic parameters potentially related with atrial fibrillation were compared between the two groups.

Statistical analysis. All analyses were performed with the SPSS 15.0 statistical package. Continuous variables were expressed as mean ± standard devia-

Table 1. Characteristics of the patients with and without atrial fibrillation (AF)

	Group I with AF (n=24)			Group II without AF (n=159)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (years)			64.9±9.8			49.9±16.6	**<0.001**
Sex							N S
Male	13	54.2		80	50.3		
Female	11	45.8		79	49.7		
Body surface area (m^2)			1.74±0.25			1.74±0.23	N S
Duration of hemodialysis (months)			55.8±53.5			39.4±37.1	N S
Coronary artery disease	9	37.5		17	10.7		**0.008**
Hypertension	10	41.7		51	32.1		N S
Diabetes	8	33.3		47	29.6		N S
Smoking	3	12.5		8	5.0		N S
Laboratory findings							
Hemoglobin (g/dl)			12.1±1.2			11.6±1.4	N S
Albumin (g/dl)			3.6±0.4			3.9±0.5	**0.015**
Calcium (mg/dl)			8.2±1.3			8.4±0.8	N S
Phosphate (mg/dl)			4.4±1.7			4.4±1.6	N S
Parathormone (pg/ml)			346.6±275.5			362.8±277.9	N S
Total cholesterol (mg/dl)			163.3±15.8			165.3±37.0	N S
Triglyceride (mg/dl)			167.1±60.2			190.9±99.2	N S
HDL-cholesterol (mg/dl)			37.5±7.9			35.1±7.4	N S
LDL-cholesterol (mg/dl)			92.5±18.2			92.4±27.6	N S
Echocardiographic findings							
Left ventricular							
End-diastolic volume index (ml/m^2)			58.3±16.0			58.1±17.2	N S
End-systolic volume index (ml/m^2)			22.1±8.3			22.9±14.2	N S
Ejection fraction (%)			61.2±8.3			63.2±8.8	N S
Mass index (g/m^2)			168.9±41.1			149.6±40.0	0.05
Left atrium diameter (mm)			43.1±7.4			36.9±6.3	**<0.001**
Right atrium diameter (mm)			41.6±8.0			32.5±5.4	**<0.001**
E/E′			11.8±3.8			8.8±4.7	**0.008**
Pulmonary artery pressure (mmHg)			38.1±6.1			28.5±5.5	**<0.001**
Valvular calcification	10	41.7		34	21.4		**0.033**

NS: Not significant.

tion. The Student's t-test was used to compare continuous variables, and the chi-square test was used to compare categorical variables between the groups. A multivariate logistic regression model was used to identify significant determinants of atrial fibrillation. To prevent the inclusion of chance correlates in the final model, we employed an epidemiological approach, and factors that had been shown to be predictors of atrial fibrillation in hemodialysis patients in previous studies were accepted as potential correlates of the outcome, including age, coronary artery disease, duration of hemodialysis, serum albumin level, systolic blood pressure, left atrial diameter, right atrial diameter, LV mass index, valvular calcification,[3-9] E/E' ratio, and pulmonary artery pressure. The strength of association between variables and the presence of atrial fibrillation was expressed by odds ratios (OR) with 95% confidence intervals (CI). A p value of less than 0.05 was considered significant.

RESULTS

Twenty-four patients (13.1%) had atrial fibrillation (group I), being permanent in 15 patients (62%), paroxysmal in seven patients (29.2%), and persistent in two patients (8.3%).

Clinical and echocardiographic findings of the two groups are summarized in Table 1. Compared with group II, patients in group I were significantly older (64.9±9.8 *vs*. 49.9±16.6 years; p<0.001) and duration of dialysis therapy tended to be longer (55.8±53.5 *vs*. 39.4±37.1 months; p=0.09). The frequency of coronary artery disease was significantly higher (37.5% *vs*. 10.7%; p=0.008) and serum albumin level was lower in group I (3.6±0.4 *vs*. 3.9±0.5 mg/dl; p=0.015). Other clinical and laboratory findings were similar (Table 1).

Echocardiographic findings. Left ventricular end-diastolic and end-systolic volumes and LV ejection

Table 2. Multivariate logistic regression analysis for prediction of atrial fibrillation in hemodialysis patients

	Odds ratio	95% confidence interval	*p*
Age	1.09	1.00 - 1.17	**0.036**
Right atrium diameter	1.19	1.05 - 1.35	**0.008**
Left atrium diameter	0.98	0.86 - 1.12	0.733
Left ventricle mass index	1.00	0.98 - 1.03	0.665
E/E′	1.05	0.90 - 1.22	0.534
Pulmonary artery pressure	1.10	0.96 - 1.26	0.151
Valvular calcification	0.92	0.19 - 4.44	0.918
Coronary artery disease	0.30	0.05 - 1.90	0.204
Duration of hemodialysis	1.00	0.98 - 1.02	0.559
Systolic blood pressure	0.97	0.92 - 1.02	0.220
Albumin	1.25	0.22 - 7.14	0.804

fraction were similar in the two groups. Left and right atrial diameters were significantly higher in group I ($p<0.05$). Left ventricular mass index was higher in the group I, but this difference did not reach statistical significance ($p=0.05$). The incidence of mitral and/or aortic calcification was significantly higher ($p=0.033$), and systolic pulmonary artery pressure (38.1±6.1 *vs*. 28.5±5.5 mmHg, $p<0.001$) and E/E' ratio (11.8±3.8 *vs*. 8.8±4.7, $p=0.008$) were significantly greater in group I.

Multivariate logistic regression analysis showed that age (OR 1.09; 95% CI 1.00-1.17; $p=0.036$) and right atrial diameter (OR 1.19; 95% CI 1.05-1.35; $p=0.008$) were independent risk factors for the development of atrial fibrillation in hemodialysis patients (Table 2).

DISCUSSION

The prevalence of atrial fibrillation was 13.1% in our study. Age and right atrial diameter were shown to be independent predictors of atrial fibrillation in hemodialysis patients. Although systolic pulmonary artery pressure and E/E' ratio were higher in patients with atrial fibrillation, these echocardiographic parameters were not independent predictors.

Atrial fibrillation is one of the most commonly encountered arrhythmia in hemodialysis patients. The prevalence of atrial fibrillation is greater in patients with chronic renal insufficiency, compared to age- and sex-matched subjects with normal renal function[4,21] and this range is highly variable (7.0% to 27.0%).[4-10] In addition, the incidence of atrial fibrillation was estimated to be 1-4.1 per 100 patient-years in this population.[2,21] Several predisposing factors and associated conditions have been reported in previous studies for atrial fibrillation seen in hemodialysis patients.[4-11,22] Among them, advanced age, concomitant coronary artery disease, atrial dilatation, predialysis systolic blood pressure, low serum albumin, and duration of hemodialysis treatment were found as independent risk factors for atrial fibrillation.[4-11,22]

In agreement with previous studies,[4-10] the prevalence of atrial fibrillation in chronic hemodialysis patients was 13.1% in our study. Increasing age is one of the most important risk factors for the development of atrial fibrillation in both the general population and hemodialysis patients.[4,5,7-9,13] In our study, the mean age of patients with atrial fibrillation was markedly higher, and age was an independent risk factor for the development of atrial fibrillation.

The relationship between atrial dilatation and atrial fibrillation has been well-established. Atrial dilatation can be a cause of atrial fibrillation, but it can also be induced by atrial fibrillation. The mechanisms responsible for this vicious cycle are not yet fully understood. In our study, both left and right atrial diameters were significantly increased in group I. In accordance with the findings of Atar et al.[5] we also showed that right atrial diameter was an independent risk factor for the development of atrial fibrillation in hemodialysis patients.

Pulmonary artery pressure is elevated and represents an independent predictor of mortality in hemodialysis patients.[23,24] The E/E' ratio shows a strong correlation with invasively measured LV filling pressure.[14] It has been demonstrated that this index is useful in predicting the risk for atrial fibrillation in patients with acute anterior myocardial infarction[15] and hypertensive patients.[16] However, the association between atrial fibrillation, E/E' ratio, and pulmonary artery pressure has not been investigated in hemodialysis patients. In our study, both pulmonary artery pressure and E/E' ratio were significantly higher in

patients with atrial fibrillation, but these echocardiographic parameters lost their statistical significance after incorporating them in multivariate regression analysis.

Concomitant coronary artery disease, valvular calcification, left ventricular hypertrophy, longer duration of renal replacement therapy, and lower albumin level have been demonstrated as risk factors for atrial fibrillation in hemodialysis patients.[4-7,9,11,21,25] These risk factors were found to be significantly different between the two groups in our study, but none was an independent predictor of atrial fibrillation in logistic regression analysis. This may result from the relatively small number of the study group and short duration of hemodialysis therapy.

Its cross-sectional design and relatively small population size are among limitations of the present study. Patients could not be followed-up prospectively in terms of new developing and/or recurrent atrial fibrillation. Further prospective studies are needed to establish the possible causal relationships between risk factors and atrial fibrillation in hemodialysis patients.

In conclusion, besides previously defined risk factors, the E/E' ratio and pulmonary artery pressure were risk factors for, and age and right atrial diameter were independent predictors of, atrial fibrillation in hemodialysis patients.

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