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Atria score to predict atrial fibrillation in acute ischemic stroke patients

Akut iskemik inmeli hastalarda atriyal fibrilasyonu öngörmek için atria skoru

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SUMMARY

Objective: Atrial fibrillation is closely associated with ischemic stroke. Ischemic stroke has been shown to be more frequent in patients with atrial fibrillation than the normal population. The predictive factors of atrial fibrillation in patients with ischemic stroke have been investigated in several studies. The aim of this study is to reveal the relationship with atrial fibrillation and ATRIA score in ischemic stroke patients.
Method: 104 patients who suffered a cerebrovascular event in sinus rhythm were included in the study. Patients were divided into two groups as detected or undetected diagnosed atrial fibrillation in 24-hour Holter ECG monitoring applied during hospitalization. The ATRIA risk score was calculated for all patients.
Results: Average of ATRIA score was found to be significantly higher in the group with detected atrial fibrillation (P = 0.001). The optimal cut-off value for ATRIA score to predict atrial fibrillation was >5 with a specificity of 78.4% and a sensitivity of 83.3% (area under the curve 0.866; 95% confidence interval (CI), 0.786–0.924, p<0.001). The ATRIA score and its components had important significance in the univariate analysis. ATRIA score and ejection fraction (OR=1.360, 95% CI: 1.090-1.697, p=0.006; OR =0.900, 95% CI: 0.834-0.971, p =0.007 respectively) were observed to be associated with atrial fibrillation in the multivariate regression analysis.
Conclusions: There is an independent relationship between the ATRIA score and the development of atrial fibrillation, in patients with ischemic stroke in sinus rhythm.
Keywords: ATRIA score, atrial fibrillation, ischemic stroke

ÖZET

Amaç: Atrial fibrilasyon ile iskemik inme yakından ilişkili olup iskemik inme geçiren hastalarda atriyal fibrilasyon ataklarının normal popülasyona oranla daha fazla olduğu gösterilmiştir. İskemik inme geçiren hastalarda atriyal fibrilasyonu ön gördürücü etkenler birçok çalışmada araştırılmıştır. Bu çalışmanın amacı da iskemik inme hastalarındaki ATRİA skorlama sisteminin atriyal fibrilasyonla ilişkisini ortaya koyabilmektir.
Yöntem: Çalışmaya sinüs ritminde serebrovasküler olay geçiren 104 hasta dahil edildi. Hastalar hastanede yatış esnasında uygulanan 24 saatlik holter EKG takiplerinde atriyal fibrilasyon atağı olanlar ve olmayanlar olarak iki gruba ayrıldı. Tüm hastaların ATRİA skorları hesaplandı.
Bulgular: ATRİA skor ortalaması atriyal fibrilasyon tespit edilen grupta anlamlı oranda yüksek bulundu. (p = 0.001) ATRİA skorunun atriyal fibrilasyonu predikte ettiği cut-off değeri %83.3 sensitivite ve %78.4 spesifite ile 5 bulundu (AUC=0,866; %95 CI, 0.786-0.924, p<0.001). ATRİA skoru ve komponentleri tek değişkenli analizde önemli prognostik öneme sahipti. Çok değişkenli regresyon analizinde, ATRİA skoru ve ejeksiyon fraksiyonun (OR=1.360, 95% CI: 1.090-1.697, p=0.006 ;OR =0.900, 95% CI: 0.834-0.971, p =0.007 sırası ile) atriyal fibrilasyon atağı ile ilişkili olduğu görüldü.
Sonuç: Sinüs ritminde serebrovasküler olay geçiren hastalarda atriyal fibrilasyon gelişmesi ile ATRİA skoru arasında bağımsız bir ilişki vardır.
Anahtar sözcükler: ATRİA skoru, atriyal fibrilasyon, iskemik serebrovasküler olay

INTRODUCTION

Ischemic strokes are responsible for 20% of cardioemboli[1]. Atrial fibrillation has an important place in the etiology of cardioemboli and atrial fibrillation is seen in half of cardio embolic patients. Additionally, atrial fibrillation is responsible not only for cardio embolic strokes but also one-sixth of all strokes. Moreover, the presence of atrial fibrillation increases the risk of stroke five times[2]. Because of the fact that atrial fibrillation and ischemic stroke are so closely associated, there has been a focus on the relationship between atrial fibrillation and stroke. Atrial fibrillation was shown to be more frequent in ischemic stroke patients than the normal population[3]. Identifying atrial fibrillation attacks in patients who have a high risk for atrial fibrillation can prevent possible morbidity and mortality due to stroke.

CHA_2DS_2-VASc score is used for both the risk and treatment planning in stroke patients. It has been shown that newly developed ATRIA score has do better risk assessment than CHA_2DS_2-VASc in the recently held two large community-based registry studies [4-5]. Each component which constitutes these risk scoring systems is an independent risk factor for atrial fibrillation. The predictive factors of atrial fibrillation in patients with ischemic stroke have been investigated in several studies [6-9]. In this study, we investigated the relationship between the ATRIA score and atrial fibrillation in patients with ischemic stroke in sinus rhythm .

MATERIAL AND METHODS

Study Population:

For this prospective study 104 patients who hospitalized with a diagnosis of ischemic stroke were included. Inclusion criteria were determined as being older than 18 years of age and written consent to participate in the study was taken. The patients who had atrial fibrillation in ECG, mechanical prosthetic valves, previously known paroxysmal atrial fibrillation, severe valve stenosis and regurgitation, patients who cannot be followed by Holter ECG and patients who found out to have atrial septal defect and patent foramen ovale in echocardiography control were not included in the study.

All patients underwent echocardiographic examination and 24-hour Holter ECG follow-up by a cardiologist.

Basic demographic and clinical data (age, sex, hypertension, diabetes mellitus, coronary heart disease, heart failure, stroke or ischemic attack and tobacco use) of the study population were recorded. ATRIA and CHA2DS2-VASc scores of all patients were calculated. Urinary proteinuria was measured for atria scoring and glomerular filtration rate was calculated at admission. Components of ATRIA and CHA_2DS_2-VASc scoring systems are shown in Table 1.

Table-1 ATRIA and CHA2DS2-VASc SCORE

Stroke Risk Stratification With The ATRIA Score		
Risk Factor	Score Without Prior Stroke	Score With Prior Stroke
Age ≥ 85	6	9
Age 75-84	5	7
Age 65-74	3	7
Age <65	0	8
Female sex	1	1
Diabetes mellitus;	1	1
Congestive heart failure	1	1
Hypertension	1	1
Proteinuria	1	1
eGFR < 45 mL/min/1.73 m2 or ESRD	1	1
Stroke Risk Stratification With The CHA2DS2-VASc		
Risk factor	Score	
C – Congestive heart failure;	1	
H-Hypertension	1	
A- Age ≥75	2	
D- Diabetes mellitus	1	
S-Stroke	2	
V- Vascular disease (prior MI, PAD, or aorticplaque)	1	
A- Age 65-74	1	
S- Sex Female	1	

Abbreviations: ATRIA, Anticoagulation and Risk Factors in Atrial Fibrillation; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease

In order to perform the 24 h Holter monitoring, the 3-Channel recordings with standard settings (Walk 400h Cardioline, Milan, Italy) were used. The recordings gained from patients for the presence of <30-s-long or ≥30-s-long AF episodes were evaluated by an experienced cardiologist who had no information about the characteristics of patients. Supraventricular runs with >3 beats, lasting <30 s with absolutely irregular RR interval and no distinct p-waves were contemplated as non-sustained AF. Self-terminating episodes which had similar morphological characteristics and lasting ≥30 s were regarded as paroxysmal AF.

Standard Echocardiography

Transthoracic echocardiographic examinations was undertaken by experienced echocardiographers who had no information about the clinical details of each subject using the Vivid 7® cardiac ultrasonography system (GE VingMed Ultrasound AS; Horten, Norway) with 2.5- to 5-MHz probes. For each patient, the left lateral and supine positions by 2D, M-mode, pulsed, and color flow Doppler echocardiography examination was carried on. Single lead electrocardiogram was unceasingly recorded. The average of at least three cardiac cycles was obtained for all measurements. The basis of examination of M-mode measurements and conventional doppler echocardiographic examinations was performed according to European Society of Echocardiography guideline criteria[10]. Doppler tracings and two-dimensional images were obtained from parasternal long and short axes, apical and subcostal views. Measurement of left and right atrial dimension, end-systolic and end-diastolic dimensions of left ventricle (LV), diastolic LV posterior, and septal wall thicknesses was carried on. Estimation of LV ejection fraction (EF) was done through Simpson's rule and measurement of left atrial volumes was conducted through disc method.

Statistical Analysis

For data management and analysis the SPSS program version 14 (SPSS Inc., Chicago, IL, USA) was used and a two-sided p-value $\leq$ 0.05 was found out to be statistically significant. Categorical variables were shown as the number of cases plus percentage and continuous variables as mean ± standard deviation (SD) or median and interquartile ranges (IQR), where usable. An independent sample t test was used for comparison of means and a Mann–Whitney U test was used with median if there was no normal distribution. The chi square test was used for appropriate categorical data evaluation. Pearson correlation test was used for normally distributed variables and for non-normally distributed variables for correlation analysis performance, Spearmen correlation test was used. Identification of the optimal cut-off point of ATRIA score for the prediction of AF was done through receiver operator characteristic (ROC) curve analysis. ROC curve analysis was done using MedCalc (v12.7.8). The area under the curve (AUC) with 95% confidence interval was estimated in prediction of AF. The optimal cutoff value of ATRIA score was identified as the value parallel with the highest sum of sensitivity and specificity-1. Univariate analysis was used for quantification of the relationship of variables with AF. The variables found out to be statistically significant in the univariate analysis and other potential confounders were used in multivariate logistic regression model with backward stepwise method for identifying independent prognostic factors of AF.

RESULTS

Upon the analysis of Holter ECG recordings of 104 patients included in the study, 18 patients were detected to have AF attacks, while 88 patients had sinus rhythm. Among patients with AF attacks, 3 of them had PAF and 15 of them had non-sustained AF.

Clinical, laboratory and echocardiographic data of two groups were formed according to the presence of AF were shown in Table 2. Coronary artery disease, proteinuria, previous stroke, age, CHA_2DS_2-VASc and ATRIA score were significantly higher in the group developing AF attacks, but there were no significant differences between groups regarding sex and other laboratory findings. Among standard echocardiographic measurements, left atrial dimensions were significantly increased and EF decreased in the group with AF attacks.

Table 2 : Baseline characteristics of study patients.

	Without AF Attacks (n= 88)	AF Attacks (n = 18)	p
Age,years	63±11	72±12	0.04
CHA2DS2-VASc score	2(1-3)	4(2.75-5)	<0.001
ATRIA score	3(1-5)	6(4-7.5)	<0.001
Hypertension, n (%)	40(45%)	8(44%)	0.938
Diabetes mellitus, n (%)	33(38%)	9(50%)	0.325
Female/ Male,(n %)	37/51	10/8	0.429
Proteinuria (n%)	4(5%)	4(22%)	0.027
Previous stroke (n%)	0	4(22%)	<0.001
Coronary Artery Disease/ Peripheral Artery Disease(n)	22(25%)	10(55%)	0.010
Blood glucose,mg/ dL	108(98-148)	143(95-157)	0.310
BUN, mg/dL	24(15-35)	17.5 (13.75-28.25)	0.126
Creatinine, mg/dL	0.85(0.61-1.1)	0.89(0.71-1.0)	0.610
Uric acid, mg/dL	5.0 ±1.6	5.2±1.5	0.747
Sodium, mg/dL	139.8 ±3.2	140±2	0.315
Potassium, mg/dL	4.8±0.43	4.7±0.13	0.560
Hemoglobin , g/dL	13.9±2.2	13.2±2.07	0.266
Echocardiographic Parameters			
EF, %	58(55-65)	55(43-85)	<0.001
LVDD, mm	4.2±0.46	4.02±0.45	0.33
LVSD, mm	3.3±0.57	3.1±0.63	0.21
LA diameter, cm	3.5 ±0.3	3.8 ±0.3	<0.01

EF: Ejection fraction, LVDD: Left ventricule end diastolic dimension , LVSD: Left ventricule end systolic dimension , LA: Left atrium, Data are presented as mean ± standard deviation (SD) number and percentage, or median and interquantile range (IQR). $p \leq 0.05$ was considered statistically significant.

It was found out that ATRIA score was positively correlated with hypertension, diabetes mellitus, age, left atrial diameter, CHA_2DS_2-VASc score and coronary artery disease while it was negatively correlated with ejection fraction (Table 3).

Table 3. Correlation co-efficients for ATRIA SCORE

Variables Correlating with ATRIA SCORE		
	R	P
Age	0.827	<0.001
Diabetes mellitus	0.278	0.009
Hypertension	0.301	0.004
CHA2DS2-VASc	0.864	<0.001
Ejection fraction	-0.524	<0.001
LA diameter	0.505	<0.001
Coronary Artery Disease	0.215	0.044

Optimal cut-off time of ATRIA score to predict AF was found to be >5 ms, with specificity of 83.3% and sensitivity of 78.4% (AUC = 0.866; 95% CI, 0.786–0.924; $p < 0.0001$ (Figure 1).

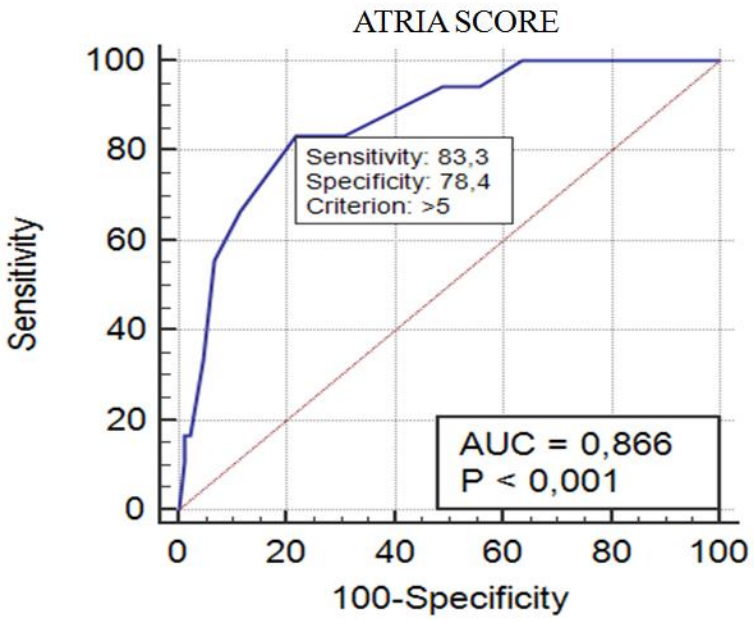

Figure-1: Receiver operator characteristic (ROC) Curve of ATRIA score to predict AF.

In the multiple logistic regression model using a back ward stepwise method, ATRIA score (OR = 1.360, 95% CI: 1.090–1.697, $p = 0.006$) and EF (OR = 0.900, 95% CI: 0.834–0.971 $p = 0.007$) still remained significant predictors of AF after adjusting for the confounding variables, which were either found to be statistically significant in the univariate analysis and for the variables correlated with the ATRIA score (Table 4).

Table 4. Univariate and multivariate analysis for predicting atrial fibrillation

	Univariate Analysis			Multivariate Analysis		
	P	OR	%95 CI	P	OR	%95 CI
ATRIA SCORE	<0.001	1.429	1.172-1.743	0.006	1.360	1.090-1.697
Ejection fraction	0.001	0.885	0.825-0.950	0.007	0.900	0.834-0.971
CHA2DS2-VASc	<0.001	2.003	1.364-2.941			
Previous Stroke	0.019	2.058	1.041-3.005			
Age	0.003	1.077	1.020-1.136			
Coronary Artery Disease/ Peripheral Artery Disease	0.001	17.000	4.469-64.671			
Proteinuria	0.019	6.000	1.343-26.808			
LA diameter	0.001	11.403	2.690-48.336			
Variables which correlated with epicardial adipose tissue						
Hypertension	0.006	6.282	1.697-23.259			
Diabetes mellitus	0.006	4.781	1.559-14.657			

All the variables from Table 1 were examined and only those significant at a $p < 0.05$ level and those with a correlated ATRIA SCORE level are shown in univariate analysis.
The multivariate logistic regression model included all univariate predictors and those with correlated ATRIA SCORE level.
CI: Confidence interval; OR: Odds ratio, Abbreviations in Table 2.

DISCUSSION

In this study, we found out that ATRIA score was independently related to AF attacks detected by 24-h Holter ECG recordings patients who with acute stroke in sinus rhythm. CHA_2DS_2-VASc score is used to evaluate the cardioemboli risk in patients with AF and to plan treatment while ATRIA score is used for risk assessment of cardioemboli. The parameters such as age, sex, diabetes mellitus, congestive heart failure, arterial hypertension, coronary artery disease located in each scoring systems are also independent predictors for atrial fibrillation development[11-13]. It is an expected finding that these scoring systems had predicted atrial fibrillation. Indeed, it is shown that CHA_2DS_2-VASc and CHADS scores predicted atrial fibrillation in patients who had ischemic stroke or not[9, 14-15]. A study conducted by Liu et al. with 1315 patients revealed that CHA_2DS_2-VASc score was an independent predictor of atrial fibrillation. In our study, it was found out that there was no predictor for atrial fibrillation in multivariate analysis although it was found out to be significant in univariate analysis. This can be explained that the small number of patients were included in the study. Another reason may be that diabetes mellitus, congestive heart failure, and arterial hypertension which are the components of CHA_2DS_2-VASc score were similar in both groups. In our study, ATRIA score was used as well as the CHA_2DS_2-VASc score. It was found out that if ATRIA score was 5 or higher in ischemic stroke patients, it was an independent predictor for atrial fibrillation attacks. There were made a more detailed classification for age in ATRIA score unlike CHA_2DS_2-VASc and CHADS scores and the points given to age was higher than the other components. Revised cerebrovascular events were evaluated in combination with age in contrast with other scoring systems. Making the age criteria which is the leading risk factor forefront can explain the fact that ATRIA score is an independent predictor for atrial fibrillation in our study. Additionally, giving the second highest score for age to the patients who had stroke younger than 65 years age may have helped to predict paroxysmal atrial fibrillation. In our study, three patients were observed to have paroxysmal atrial fibrillation attacks and those patients were under 65 years age. In our study, there was no relation between hypertension, diabetes mellitus, heart failure and history of stroke and atrial fibrillation in multivariate analysis although there was a strong relation in univariate analysis. This can be explained by the fact that the number of patients included in the study was low and the prevalence of these diseases was high in the study group. On the other hand, it was found that low EF was associated with atrial fibrillation in both univariate and multivariate analysis. Another important risk factor for atrial fibrillation is heart failure. Intra-cardiac pressure increase causes atrial wall tension and remodeling in atrial wall in heart failure and predisposes to atrial fibrillation[16]. Consistent with the literature, our study also revealed that EF decrease was found as an independent predictor for atrial fibrillation in patients who has cerebrovascular events.

CONCLUSION

As the result, following the rhythm of the patients who had cerebrovascular events in sinus rhythm with high Atria score will not only help the diagnosis of atrial fibrillation but also decrease unnecessary labor force and the cost.

LIMITATIONS

The main limitation of this study is that it is a cross-sectional study and Holter ECG following was done just in the first day of hospitalization. Long-term rhythm follow-up was not done when atrial fibrillation attacks were determined in Holter ECG. Additionally, the small number of patients and being one-centered is another limitation of our study. More accurate results can be obtained with long-term follow-up and higher number of patients.

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