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A Simple Risk Scoring Systems to evaluate the presence of aneurysm and one-year mortality in patients with abdominal aortic aneurysm using CHA2DS2-VASc and ATRIA

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SUMMARY

OBJECTIVE: We aimed to demonstrate the clinical utility of CHA_2DS_2-VASc and anticoagulation and risk factors in atrial fibrillation risk scores in the assessment of one year mortality in patients with abdominal aortic aneurysm.

METHODS: We designed a retrospective cohort study using data from Suleyman Demirel University Hospital for the diagnosis of abdominal aortic aneurysm. The study included 120 patients with abdominal aortic aneurysm who underwent aortic computed tomography. Patients were divided into two groups according to presence of abdominal aortic aneurysm and the development of mortality. Predictors of mortality were determined by multiple logistic regression analysis.

RESULTS: Multivariate regression analysis showed that CHA_2DS_2-VASc score, advanced age, female gender and elevated white blood cell counts were independent predictors of abdominal aortic aneurysm development while CHA_2DS_2-VASc score and elevated glucose levels were independent predictors of one year mortality in patients with abdominal aortic aneurysm. The concordance statistics for anticoagulation and risk factors in atrial fibrillation risk Score and CHA_2DS_2-VASc risk score respectively were 0.96 and 0.97 and could significantly predict one year mortality in patients with abdominal aortic aneurysm ($p<0.001$, and $p<0.001$, respectively).

CONCLUSIONS: CHA_2DS_2-VASc and anticoagulation and risk factors in atrial fibrillation risk scores are easily obtained in an emergency setting and can accurately predict one year mortality as a noninvasive follow-up in patients with abdominal aortic aneurysm. These simple scores could be used as a point of care decision aid to help the clinician in counseling patients presenting with abdominal aortic aneurysm and their families on treatment protocols.

KEYWORDS: Aortic aneurysm. Abdominal. Mortality. Risk assessment. Methods.

INTRODUCTION

Abdominal aortic aneurysm (AAA), which is characterized by abnormal focal dilation of the abdominal aorta, is relatively common and is associated with significant morbidity and mortality. AAA, whose prevalence increases with age, is the most common vascular disease of the abdominal aorta in clinical practice, affecting 3% of the population aged over 50 years[1,2]. Although most AAA patients are asymptomatic, some patients are admitted to the emergency services for life-threatening symptoms and have an in-hospital mortality of about 40%. Therefore, foreseeing the development of aneurysm and regression could be beneficial for survival. Recent studies have demonstrated a strong association between AAA and cardiovascular risk factors[3,4].

The CHA_2DS_2-VASc and Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) risk scores are simple and effortless scoring systems that are used to predict the risk of thromboembolism in non-valvular atrial fibrillation (AF) patients[5,6]. Additionally, these scoring systems have been associated with

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worse clinical outcomes in patients with acute coronary syndrome regardless of the presence of AF[7,8].

The aim of the study was to evaluate whether CHA_2DS_2-VASc and ATRIA risk scores could accurately predict AAA and 12-month mortality after discharge of AAA patients.

METHODS

Patients

In this observational and cross-sectional study, we retrospectively screened data from patients with intact infrarenal AAA who were admitted to either the Emergency Department or the Outpatient Clinics at Suleyman Demirel University Education and Research Hospital between January 2014 and August 2019. Cases were excluded if they had incomplete clinical or para-clinical data, infectious aneurysms, need for preoperative resuscitation, ruptured/symptomatic AAA or previous endovascular treatment. The extracted clinical data included gender, age, size of the aneurysm, presence of hypertension, diabetes, chronic renal failure, heart failure, cerebrovascular event, peripheral vascular disease, hospitalization duration, and in-hospital mortality rate. The aneurysm size was measured on preoperative computed tomography angiograms. The study was approved by the medical ethical committee of Suleyman Demirel University's School of Medicine and all patients signed a written informed consent (Decision N° 13.12.2018-247). A total of 178 patients were screened and 58 subjects were excluded after applying the exclusion criteria. The final study group consisted of 120 patients who met the inclusion and exclusion criteria. Patients were divided into two groups according to the presence of AAA.

Statistical analysis

All calculations were performed using the Statistical Package for Social Sciences software, SPSS 16.0 (SPSS Inc, Chicago, Illinois). Continuous variables were expressed as mean (standard deviation) or median (interval between quartiles); categorical variables were expressed as frequency (%) and numbers. Kolmogorov-Smirnov test was used in the evaluation of normality. Continuous variables were compared using the Mann-Whitney U test or the Student's *t*-test, whereas categorical variables were compared using the χ^2 test or the Fisher test. In all statistical analyses, $p<0.05$ was considered as statistically significant. The correlations were analyzed through Pearson or Spearman correlation analyses where appropriate. To investigate the association between the variables, AAA, and one year mortality, univariate regression analysis was performed, and variables with $p<0.10$ were performed in the multivariate logistic regression analysis. Receiver operating characteristics (ROC) curve analysis was performed to analyze the prognostic value of ATRIA and CHA_2DS_2-VASc risk scores for detecting AAA and one-year mortality. C-Statistic (area under the curve) was presented as a unified estimate of sensitivity and specificity.

Clinical outcomes and definitions

One year after discharge, the patients were investigated for the cause of death (cardiac or non-cardiac) via telephone calls. Computer assisted tomography was used to visualize the aorta and to determine the maximal aneurysm diameter. A diameter of 35 mm or more at the level of the infrarenal abdominal aorta was defined as an abdominal aortic aneurysm. The CHA_2DS_2-VASc and ATRIA scores were calculated as stated in previous studies[5,6].

RESULTS

A total of 120 patients (mean age: 64±12 years; range, 35–95 years) were included in this study. During the follow-up period, 25 patients (20.8 %) died. The demographic and clinical characteristics of patients with and without aneurysm are listed in Table 1. The demographic and clinical characteristics of aneurysm patients with and without mortality are listed in Table 1. Patients with aneurysm had significantly higher mean CHA_2DS_2-VASc (2.6±1.9 *versus* 1.4±1.3, $p<0.001$) and ATRIA scores (5.0±3.7 *versus* 4.3±2.7 *versus*, $p<0.001$) compared to patients without aneurysm. The mean CHA_2DS_2-VASc and ATRIA scores were significantly higher in patients with mortality compared to patients without mortality (4.9±1.2 *versus* 1.4±0.9, $p<0.001$; 9.2±2.2 *versus* 2.9±2.2, $p<0.001$; respectively). A multivariate binary logistic regression analysis was carried out by including all characteristics associated with the development of AAA in the univariate analysis (Table 2). This analysis showed that CHA_2DS_2-VASc score (OR=1.39; 95%CI 1.08–1.80, p=0.01), female gender (OR=2.92; 95%CI 1.25–6.82, p=0.01), and white blood cell count (OR=1.11; 95%CI 1.03–1.20, p=0.006) remained as independent risk factors for AAA development. ROC curve analysis showed that both ATRIA score (C-statistic: 0.68; 95%CI 0.59–0.78, $p<0.001$) and CHA_2DS_2-VASc score (C-statistic: 0.67; 95%CI 0.58–0.77, p=0.001) were significant predictors of AAA. We calculated that a cut-off point of 3.5 for ATRIA and 1.5 for CHA_2DS_2-VASc scores could estimate the development of AAA with a sensitivity of 58 and 70% and a specificity of 66 and 65%, respectively. A pair-wise comparison of ROC curves indicated that the predictive value of the ATRIA risk score and CHA_2DS_2-VASc score were similar for the prediction of AAA development (AUC ATRIA *versus* AUC CHA_2DS_2-VASc, z test=0.561, p=0.574; DeLong method). A multivariate binary

logistic regression analysis was carried out by including all characteristics that were associated with mortality in patients with AAA in the univariate analysis (Table 2). This analysis showed that a high CHA_2DS_2-VASc score (OR=29.04; 95%CI 2.34–359.09, p=0.009) and glucose level (OR=1.02; 95%CI 1.00–1.05, p=0.05) remained as independent risk factors for mortality in patients with AAA (Table 2). ROC curve analysis showed that both ATRIA score (C-statistic: 0.96; 95%CI 0.91–1.00, p<0.001) and CHA_2DS_2-VASc score (C-statistic: 0.97; 95%CI 0.93–1.00, p<0.001) were significant predictors of mortality in patients with AAA (Figure 1). A cut-off score of 6 for ATRIA and 3 for CHA_2DS_2-VASc were calculate to be able to estimate mortality in patients with AAA with a sensitivity of 85 and 92% and a specificity of 85 and 100%, respectively. A pair-wise comparison of ROC curves was performed and estimated that the predictive value of the ATRIA and CHA_2DS_2-VASc risk scores were similar in the prediction of mortality in patients with AAA (AUC ATRIA *versus* AUC CHA_2DS_2-VASc, z test=0.974, p= 0.33, DeLong method).

DISCUSSION

The present study identified a significant relationship between CHA_2DS_2-VASc and ATRIA risk sores and the development of AAA. Moreover, the present study demonstrated that CHA_2DS_2-VASc and ATRIA risk sores could strongly predict one-year mortality in patients with AAA. Our data suggest that these scores might be used as prognostic predictors in patients with AAA.

It has been previously reported that the presence of structural diseases such as mitral annular calcification and an increase in epicardial adipose tissue were associated with high CHA_2DS_2-VASc scores[9,10]. Additionally, the same studies also showed that echocardiographic left ventricular measurements were associated with high CHA_2DS_2-VASc scores. Corroborating these data, AAA, a structural disease, was shown to be associated with a high CHA_2DS_2-VASc score. The CHA_2DS_2-VASc score was previously reported to be associated with in-hospital and long-term adverse clinical outcomes, including mortality, in patients with both stable coronary artery disease and acute coronary syndrome[11,12]. Similarly, the present study showed

Table 1. Demographic and clinical characteristics of patients with and without AAA; AAA patients with and without mortality

	Aneurysm (-) (n=60)	Aneurysm (+) (n=60)	p-value	Mortality (-) (n= 40)	Mortality (+) (n=20)	p-value
CHA2DS2-VASc score	1.4±1.3	2.6±1.9	<0.001	1.4±0.9	4.9±1.2	<0.001
ATRIA score	2.7±2.7	5.0±3.7	<0.001	2.9±2.2	9.2±2.2	<0.001
Age, years	60.7±11.0	67.7±13.2	<0.001	62.5±12.4	78.2±7.5	<0.001
Female gender n, %	15 (25)	30 (50)	0.004	18 (45)	12 (60)	0.224
Hypertension n, %	41 (68.3)	49 (81.7)	0.07	29 (75)	20 (100)	0.007
Diabetes mellitus n, %	11 (18.3)	19 (31.7)	0.07	5 (12.5)	14 (70)	<0.001
Stroke–TIA n, %	5 (8.3)	17 (28.3)	0.004	1 (2.5)	16 (80)	<0.001
Mortality n, %	5 (8.3)	20 (33.3)	0.001			
Hemoglobin (mg/dL)	13.4 (2.4)	12.1 (2.3)	0.004	12.6±2.2	11.0±2.3	0.01
White blood cell	8743±4100	12258±3500	0.001	11.9±6.8	12.8±5.9	0.643
Platelet	222474±12580	236236±11700	0.484	245±108	257±131	0.710
Glucose (mg/dL)	121±45.6	122±45.6	0.959	106±33.1	153±51.6	<0.001
Creatinin (mg/dL)	1.2±1.0	1.2±0.7	0.979	1.0±0.3	1.5±1.1	0.03
Total cholesterol (mg/dL)	200.2±41.2	190.9±38.1	0.310	195.4±35.2	193.2±32.1	0.560
HDL cholesterol (mg/dL)	40±8.0	41±7.5	0.790	39.0±9.1	40±7.5	0.760
LDL cholesterol (mg/dL)	125±29	127±35	0.915	107±47	92±43	0.245
Triglycerides (mg/dL)	156±95	136±32	0.105	154.0±65	140.1±52	0.260
LV ejection fraction (%)	60.1±0,3	60.2±0,3	0.962	60.2±0,3	60.7±0,3	0.480
Aneurysm diameter (mm)	20.72±1.3	53.63±7.2	<0.001	53.8±7.5	53.2±6.8	0.776

Data presented as mean ± standart deviation or number (%) of the patients; CHA2DS2-VASc: congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke, vascular disease, age 65 to 74 years, female gender; ATRIA: Anticoagulation and risk factors in atrial fibrillation risk score; TIA: Transient ischemic attack; LV: Left ventricular.

that high scores may also be related to one-year mortality. Moreover, these scores were associated with contrast-induced nephropathy and poor coronary perfusion after primary percutaneous coronary intervention[13,14]. The CHA_2DS_2-VASc score, which was created from $CHADS_2$, is recommended in contemporary guidelines for appraising oral anticoagulant therapy in patients with non-valvular AF[6]. Although the underlying mechanisms of AAA are not fully understood, previous studies have shown that systemic processes often caused alterations in the vascular wall, leading to a loss of vascular structural proteins and wall strength. Older age, male gender, cigarette smoking, Caucasian race, atherosclerosis, hypertension, family history of AAA, and other large artery aneurysms are the most important risk factors for the development of AAA[15]. The CHA_2DS_2-VASc and ATRIA scores evaluate similar risk factors for AAA; suggesting that these scores can be used to predict the risk of AAA[16]. To the best of our knowledge, no published study has investigated the relationship between AAA and the CHA2DS2-VASc score.

Although most AAA patients are asymptomatic, rupture is a mortal complication of AAA and has an in-hospital mortality rate of about 50%. Even if patients are operated on, surgery-related mortality has been reported to be up to 70%[15,17]. However, the elective surgery mortality rates were reported to be lower than emergent surgery mortality rates[17,18]. Reliable prediction of outcomes in patients with AAA and efficient follow-up are very important to reduce mortality and decrease healthcare costs. Edinburgh Ruptured Aneurysm Score (ERAS), Hardman Index (HI), and Glasgow Aneurysm Score (GAS) are the three risk evaluation scores that have been established to predict the development of AAA[19,20]. However, Gatt et al.[21] showed that HI and GAS were weak predictors of outcome after rupture of AAA

Table 2. Predictors of AAA and mortality in univariate and multivariate regression analysis

	Univariate analysis for AAA presence			Multivariate analysis for AAA presence			Univariate analysis for mortality			Multivariate analysis for mortality		
	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value	OR	95%CI	p-value
ATRIA risk score	1,237	(1.097–1.394)	0.001				2.49	(1.56–3.97)	<0.001			
CHA2DS2VASC risk score	1.516	(1.190–1.932)	0.001	1.39	(1.08–1.807)	0.01	15.13	(2.34–97.59)	0.004	29.04	(2.34–359.09)	0.009
Age	1.048	(1.016–1.081)	0.003				1.14	(1.06–1.22)	<0.001			
Female gender	3.00	(1.38–6.4)	0.005	2.92	(1.25–6.82)	0.01						
Hypertension	2.06	(0.88–4.83)	0.095									
Diabetes Mellitus	2.06	(0.88–4.83)	0.095					16.33	(4.28–62.31)	<0.001		
Stroke/TIA	4.34	(1.48–12.7)	0.007									
Hemoglobin	0.80	(0.68–0.93)	0.005					0.71	(0.55–0.93)	0.014		
White blood cell	1.13	(0.04–1.22)	0.002	1.11	(1.03–1.20)	0.006						
Glucose							1.03	(1.01–1.05)	0.002	1.02	(1.00–1.05)	0.05
GFR							0.97	(0.94–0.99)	0.03			
Creatinine							2.41	(0.90–6.43)	0.07			

OR: odds ratio; CI: confidence interval; CHA2DS2-VASc: congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, previous stroke, vascular disease, age 65 to 74 years, female gender; ATRIA: anticoagulation and risk factors in atrial fibrillation risk score; TIA: transient ischemic attack; GFR: glomerular filtration rate.

repair and no thorough validation of ERAS has been performed in an independent cohort. A variety of scores have been evaluated in previous studies for predicting mortality risk in patients with ruptured AAA[22-24]. Healey et al.[22] showed that advanced age, elevated creatinine and low systolic blood pressure were associated with 30-day mortality in patients with ruptured AAA who were being considered for repair in the endovascular area. Wise et al.[23] determined that the GAS score could predict mortality in patients with ruptured AAA. Vos et al.[24] evaluated the presence of a relationship between the mortality risk in patients with ruptured AAA and five different aneurysm scoring systems, including GAS, HI, the Vancouver Scoring System (VSS), ERAS, and Dutch Aneurysm Score. These authors reported a statistically significant difference only between the VSS and the GAS scores in favor of the VSS. Unlike these studies, the current study reports that CHA_2DS_2-VASc and ATRIA risk scores, two simple risk models for predicting thromboembolic risk in patients with non-valvular AF, were associated with developmental aneurysm and could predict one-year mortality in patients with un-ruptured AAA. Other aneurysm scoring systems are complex and time-consuming as they also require clinical and laboratory variables that may not be available to the clinician immediately. The present study showed that, in addition to predicting the development of AAA, the CHA_2DS_2-VASc and ATRIA scores were positively correlated with the size of the aneurysm and, subsequently, with the risk of rupture. Additionally, patients with high CHA_2DS_2-VASc and ATRIA scores showed an increased risk of mortality. Therefore, patients with high ATRIA and CHA_2DS_2-VASc risk scores should be screened with ultrasonography or, if indicated, angiography. Risk modifications should be administrated to decrease morbidity and mortality.

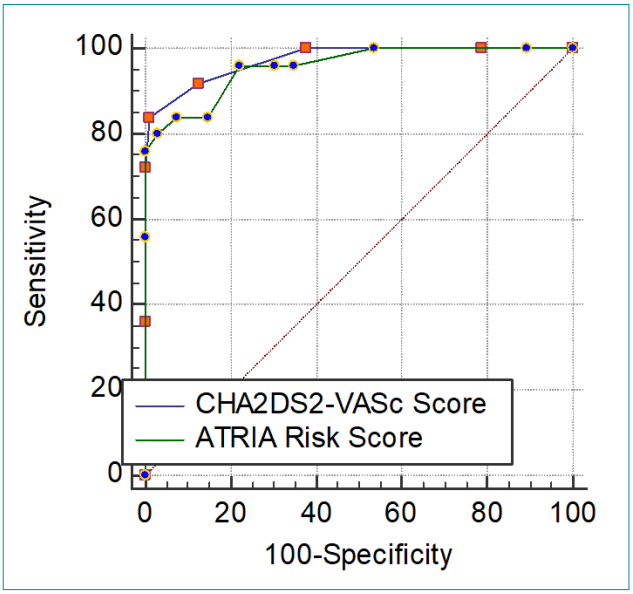

Figure 1. Receiver operating characteristic (ROC) curve with calculated area under the curve and optimal cut-off point for the CHA_2DS_2VASC score and anticoagulation and risk factors in atrial fibrillation risk score to identify the presence of one year mortality in patients with abdominal aortic aneurysm.

In conclusion, supporting our hypothesis, the current study shows that the CHA_2DS_2-VASc and ATRIA risk scores were strong independent predictors of one year mortality in patients with AAA and may identify patients who will benefit most from early invasive management. Individuals with high CHA_2DS_2-VASc and ATRIA risk scores should be advised to pay more attention to the reduction of unfavorable cardiovascular risk factors and the development of future cardiovascular events. Additionally, lifestyle changes and cardiovascular risk modifications may reduce cardiac and vascular structural changes such as left atrial dilatation, left ventricular hypertrophy, and aortic dilatation. Moreover, individuals with high CHA_2DS_2-VASc and ATRIA risk scores should undergo open or endovascular treatment to decrease the risk of rupture or should be closely monitored with frequent ultrasonography or angiography to mitigate the risk of rupture.

AUTHORS' CONTRIBUTION

FA: Conceptualization, Methodology, Project Administration, Writing-Review & Editing. **DU:** Resources, Validation, Investigation, Writing-Original Draft.

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