PREDICTING UNSUCCESSFUL ELECTRICAL CARDIOVERSION FOR ACUTE ATRIAL FIBRILLATION (FROM THE AF-CVS SCORE)

By

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ABSTRACT

Background: Despite good progress in the management of patients with atrial fibrillation, this arrhythmia remains one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world. Furthermore, the number of patients with AF is predicted to rise steeply in the coming years.

Objective: To validate a clinical risk stratification tool (AF-CVS score) for identifying patients at high risk for unsuccessful outcome after electrical cardio-version for acute AF.

Patients and Methods: The present study was a cohort study conducted between March 2018 and March 2019. We enrolled 100 consecutive patients admitted at Al-Hussain University, Al-Azhar University, presented with acute onset atrial fibrillation (AF) requiring direct current electro-version (DC electro-version). An informed consent obtained from every patient after full explanation of the research objectives and the purpose of this study.

Results: A binary logistic regression was run to evaluate AFCVS score as a predictor for the recurrence among the patients in the study population. There was homoscedasticity and normality of the residuals. The binary logistic regression model was statistically significant ($\chi2$= 28.01, df 1, p= < 0.001) with insignificant Hosmer and Lemeshow test (p 0.114). AFCVS score was a significant predictor for the AF recurrence in the studied population (p< 0.001). The diagnostic efficacy and cut off point of AFCVS for prediction of AF recurrence in the studied sample was determined using a receiver operating characteristic curve (ROC) and the AFCVS score cut off point was 5 . The score showed 83.8% sensitivity, 68.3% Specificity, 87.8% negative predictive value, 60.8% positive predictive value and 74% accuracy.

Conclusion: Atrial fibrillation provokes important economic burden along with significant morbidity and mortality. Our study showed that the risk of unsuccessful outcome of ECV can be predicted using five simple clinical variables: A-- Age. F-- not First time AF. C-- Cardiac failure. V-- Vascular disease. S-- Short duration from previous AF (within 1 month before electrical cardio-version (ECV)).

Keywords: Electrical Cardioversion, Acute Atrial Fibrillation, AF-CVS score.

INTRODUCTION

Atrial fibrillation (AF) is the most commonly encountered arrhythmia in clinical practice. Aging populations coupled with improved outcomes for many chronic medical conditions has led to increases in AF diagnoses. AF is also known to be associated with an increased risk of adverse events such as transient ischemic attack, ischemic stroke, systemic embolism, and death *(Amin et al., 2016)*.

Atrial Fibrillation remains one of the major causes of stroke, heart failure, sudden death, and cardiovascular morbidity in the world *(Kirchhof et al., 2016)*.

Quality of life is impaired in AF patients independent of other cardiovascular conditions. About 10-40% of AF patients are hospitalized every year *(Kotecha et al., 2014)*. About 20-30% of patients with an ischemic stroke are due to AF *(Kishore et al., 2014)*. A growing number of patients with stroke are diagnosed with silent paroxysmal AF *(Stewart et al., 2012)*.

In 2010, the estimated numbers of men and women with AF worldwide were 20.9 million and 12.6 million, respectively, with higher incidence and prevalence rates in developed countries. Furthermore, the number of patients with AF is predicted to rise steeply in the coming years *(Kirchhof et al., 2016)*.

Synchronized direct current electrical cardio-version (ECV) quickly and effectively converts AF to sinus rhythm, and is the method of choice in severe haemodynamically compromised patients with new onset AF *(Kirchhof et al., 2012)*. Severity of AF symptoms and patient preference should be considered when embarking on a strategy requiring serial cardio-version procedures *(January et al., 2019)*.

Although electrical cardio-version (ECV) is the standard treatment for acute AF, the identification of patients with increased risk of ECV failure or early AF recurrence is of importance for clinical decision making. However, limited studies have been carried out to establish an association between the clinical variables and the outcome of the ECV *(Jaakkola et al., 2017)*.

The aim of this study was to validate a clinical risk stratification tool (AF-CVS score) for identifying patients at high risk for unsuccessful outcome after electrical cardio-version for acute AF.

PATIENTS AND METHODS

The present study was a cohort study conducted between March 2018 and March 2019. We enrolled 100 consecutive patients admitted at Al-Hussain University; Al-Azhar University presented with acute onset atrial fibrillation (AF) requiring direct current electro-version (DC electro-version). An informed consent was obtained from every patient after full explanation of the research objectives and the purpose of this study.

Inclusion Criteria: All patients with no contraindication for DC-Cardioversion were enrolled in the study:

- Patients with acute onset first time AF aiming at restoring sinus rhythm.

- Adult patients with documented paroxysmal AF assigned for rhythm control.

- Patients with acute onset AF not responding to pharmacological therapy.

- Patients with acute onset AF and pre-excitation with hemodynamic instability.

Exclusion Criteria:

- Any patient refused to sign an informed consent.

- All patients presented with AF who were assigned for rate control.

- Valvular heart disease other than mild mitral and tricuspid valve regurgitation.

- Rheumatic heart disease.

- Previous heart valve surgery.

- Congenital heart disease.

For each enrolled patient, the following data were collected:

History: Patients' data as gender, age (in years), smoking status, presence or absence of hypertension, diabetes mellitus, ischemic heart disease, dyslipidemia, chronic obstructive airway disease and full drug history including alcohol consumption have been recorded. Detailed history of onset and duration of AF prior to DC cardio-version, previous DC cardio-version (type, joules and post complications) and the date of follow up after the DC cardio-version. From previous data, we calculated the AF-CVS score.

AF-CVS score:

Identification of the risk of electrical cardio-version failure according to the clinical variables in the AF-CVS score which are:

A— Age: Age (years): <45 = 0 points; 45-65 = 1 point; >65 = 2 points.

F-- Not First time AF: Not the First AF episode = 2 points

C-- Cardiac failure: Cardiac failure = 2 points

1. Patients with HFPEF: patients with symptoms and signs of congestive heart failures, left ventricular ejection fraction (LVEF) >50% and non a dilated left ventricle and evidence of elevated left ventricular filling pressure.

2. Patients with HFREF: patients with impaired contractility of the left ventricle in an ejection fraction (EF) of <40% to 50%.

V-- Vascular disease: Vascular disease = 1 point

S-- Short duration from previous AF (within 1 month before electrical cardio-version (ECV)): Short interval (another AF episode within 30 days) = 3 points.

Basic examination: Clinical data as heart rate, systolic and diastolic blood pressures at rest were performed in details with: General examination, cardiac examination, weight (in Kilograms), height (in Centimeters) and body Mass Index (BMI) (in Kilograms/Square meters).

Laboratory assessment: Routine laboratory investigations were done as HBA1C, lipid profile, thyroid profile, liver function test, renal function test, and full blood picture as well as coagulation profile.

Imaging: ECG, echocardiography, chest X-ray and trans esophageal echo cardiography (TOE).

Intervention: Electrical Cardio-version

Patient preparation:

- Review of: history & physical examination, medication & anticoagulation and thromboembolic risk.

- 12 lead ECG

- Peripheral venous access

- O2 airway

- Sedation: midazolam 2mg over 2 minutes

Technique:

- Electrodes placement: patches are placed in antero-apical position

- Energy: 100 joule biphasic

- Synchronization: synchronized

Patients were followed up for 30 days after electrical cardio-version to record the symptoms, signs and persistence of sinus rhythm as well as DC-cardioversion outcome and evaluate the validity of the AF-CVS score in prediction.

Statistical analysis:

Recorded data were analyzed using the statistical package for social sciences, version 20.0 (SPSS Inc., Chicago, Illinois, USA). Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage. Independent-samples t-test of significance was used when comparing between two means. Chi-square (x2) test of significance was used in order to compare proportions between two qualitative parameters. Mann-whitney U test was used to compare AFCVS score. A receiver operating characteristic curve (ROC) was used to determine the diagnostic efficacy and cut off points of AFCVS score. The confidence interval was set to 95% and the margin of error accepted was set to 5%. $P < 0.05$ was considered significant.

RESULTS

Demographic data were presented in **Table (1)**.

Table (1): Patient demographics and medical history

		All patients (n= 100)				
		Mean & SD	**Median**	**Minimum**	**Maximum**	**IQR**
Age (years)		51.97 ± 11.356	52.50	29	78	45.00, 59.50
Height (m)		1.68 ± 0.064	1.68	1.53	1.89	1.63, 1.72
Weight (kg)		86.73 ± 16.099	85.00	55.00	120.00	75.00, 99.75
BMI		30.84 ± 5.916	30.09	18.38	46.87	26.35, 34.23
Gender	**Males**	50% (50)				
	Females	50% (50)				
Smoking		37% (37)				
Alcohol		2% (2)				
HTN		58% (58)				
DM		46% (46)				
IHD		46% (46)				
COPD		13% (13)				
OSA		13% (13)				
Data were expressed as mean and standard deviation, median, Minimum, Maximum and Inter-quartile range or percentage and frequency.						

Patients' age ranged from 29 to 78 years. 37% of them were smokers and 2% were alcoholics. Patient's height ranged from 1.53m to 1.89m. Patient's weight ranged from 55kg to 120kg. Patient's body mass index (BMI) ranged from 18.38 to 46.87. 58% of the patients were hypertensive 46% of the patients were diabetic 46% of the patients were ischemic heart disease 13% of the patients were chronic obstructive pulmonary disease 13% of the patients were obstructive sleep apnea **(Table 2)**.

Table (2): Comparison of demographic data and CVS risk factors between cases according to AF recurrence

Demographic Characteristics	No recurrence (n= 63)	Recurrence (n= 37)	t/ χ^2#	p-value
Age (years) Mean±SD Range	50.41±9.73 (29.0-69.0)	57.35±13.70 (35.0-78.0)	2.95	0.004
Sex Female Male	35(55.6%) 28(44.4%)	15(40.5%) 22(59.5%)	2.10	0.147
BMI (kg/m$^{2)}$) Mean±SD Range	31.30±5.18 (21.2-44.1)	30.06±7.02 (18.4-46.9)	1.01	0.315
AFCVS score Mean±SD Range	3.46±2.29 (0.0-8.0)	6.03±2.11 (1.0-10.0)	5.56	0.001
Smoking No Yes	**46(73.0%)** **17(27.0%)**	**17(45.9%)** **20(54.1%)**	**7.33**	**0.007**
Alcohol No Yes	62(98.4%) 1(1.6%)	36(97.3%) 1(2.7%)	FET	P=0.70
Hypertension No Yes	**40(63.5)** **23(36.5)**	**9(24.3)** **28(75.7)**	**14.31**	**<0.001**
DM -VE +VE	30(47.6%) 33(52.4%)	24(64.9) 13(35.1)	2.79	0.095
IHD No Yes	38(60.3%) 25(39.7%)	16(43.2%) 21(56.8%)	2.74	0.098

x2: Chi-square test; FET :Fischer exact test

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There was a statistically significant difference in age between patients with no AF recurrence and patients with recurrence (p value < 0.05). The recurrence group has higher age than no recurrence group.

The percentage of smokers in the AF recurrence group was significantly higher than no AF recurrence group (p value < 0.05)

There was a significant difference between both groups regarding hypertension (p value < 0.05). Percentage of hypertensive patients was higher than non-hypertensive in the recurrence group. There was a statistically significant difference (p value < 0.001) between AFCVS score value in the group with recurrent AF and group with non-recurrent AF **(Table 3)**.

Table (3): Comparison of drug history and COPD & OSA between cases according to AF recurrence

Recurrence \ Parameters	No recurrence (n= 63)	Recurrence (n= 37)	χ^2	p-value
Drug history: ACEIs	22(34.9%)	16(43.2%)	0.685	0.408
ARBs	12(19.0%)	8(21.6%)	0.097	0.756
BBs	27(42.9%)	17(45.9%)	0.09	0.764
CCBs	9(14.3%)	3(8.1%)	0.842	0.359
Digoxin	4(6.3%)	4(10.8%)	FET	0.463
Statins	34(54.0%)	24(64.9%)	1.14	0.304
Propafenone	6(9.5%)	3(8.1%)	0.057	0.811
Sotalol	00	0	0	1
Amiodarone	4(6.3%)	3(8.1%)	FET	0.708
COPD	6(9.5%)	7(18.9%)	1.82	0.177
OSA	4(6.3%)	2(5.4%)	FET	0.845

There was no statistically significant difference between recurrence and non-recurrence group regarding drug history **(Table 4)**.

Table (4): Comparison of echocardiography according to AF recurrence incidence

Recurrence \ Parameters	No recurrence (n= 63)	Recurrence (n= 37)	t-test/χ^2	p-value
LVEF (%). Mean±SD Range	59.09±6.99 (40.0-71.0)	55.65±7.56 (42.0-65.0)	2.31	0.023
RV dysfunction	9 (14.3%)	9 (24.3%)	1.59	0.207
LV size (cm). Mean±SD Range	3.27±0.38 (2.5-4.0)	3.29±0.387 2.6-4.0	0.177	0.860
RA size (cm). Mean±SD Range	2.11±0.47 (1.5-3.2)	2.24±0.54 (1.5-3.5)	1.23	0.224

t-Independent Sample t-test;

There was a statistically significant difference in LVEF of both groups. The LVEF was significantly higher in no AF recurrence group (p value < 0.05) **(Table 5)**.

Table (5): CHA2DS2_VASC and HASBLED score in the studied patients

		All patients (n= 100)
CHA2DS2_VASC	**0**	13.0% (13)
	1	18.0% (18)
	2	32.0% (32)
	3	17.0% (17)
	4	10.0% (10)
	5	10.0% (10)
HASBLED	**0**	21.0% (21)
	1	31.0% (31)
	2	26.0% (26)
	3	19.0% (19)
	4	3.0% (3)
Data was expressed as percentage and frequency.		

A binary logistic regression was run to evaluate AFCVS score as a predictor for the recurrence among the patients in the study population. There was homoscedasticity and normality of the residuals. The binary logistic regression model was statistically significant ($\chi 2$= 28.01, df 1, p= < 0.001) with insignificant Hosmer and Lemeshow test (p 0.114). AFCVS score was a significant predictor for the AF recurrence in the studied population (p< 0.001). The model classified 63% of the studied sample with Nagelkerke R2 33.4% **(Table 6)**.

Table (6): ACCVS score for recurrence prediction

|	B	P	Odds ratio	95% CI
AFCVS	0.479	**< 0.001**	1.614	1.311, 1.987

A receiver operating characteristic curve (ROC) was used to determine the diagnostic efficacy and cut off point of AFCVS for prediction of AF recurrence in the studied sample.

The diagnostic efficacy and cut off point of AFCVS for prediction of AF recurrence in the studied sample was determined using a receiver operating characteristic curve (ROC) and the AFCVS score cut off point was 5. The score showed 83.8% sensitivity, 68.3% Specificity, 87.8% negative predictive value, 60.8% positive predictive value and 74% accuracy **(Table 7** and **Figure 1)**.

Table (7): **Diagnostic values of AFCVS score**

Diagnostic values	AFCVS
Area under the curve	0.774
95% confidence interval	0.680, 0.868
Cut- off point	5 (rounded from 4.5)
Distance from the curve	0.13
Sensitivity	83.8%
Specificity	68.3%
Positive predictive value	60.8%
Negative predictive value	87.8%
Accuracy	74%
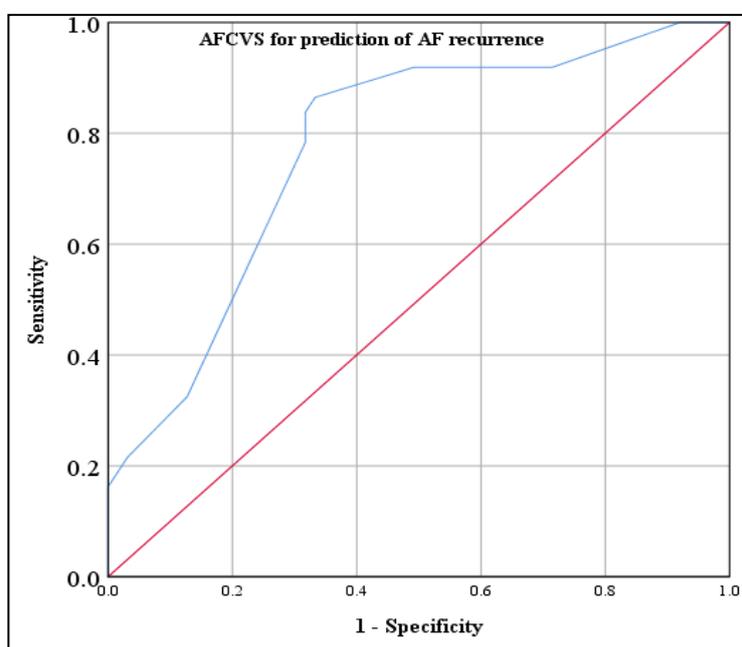
Figure (1): ROC curve for AFCVS score

DISCUSSION

We conducted our study on 100 cases of acute AF undergoing electric cardio-version either patients with acute AF to restore sinus rhythm or patients with acute AF not responding to pharmacological therapy or patients with acute AF and pre-excitation with hemodynamic instability.

Patients' age ranged from 29 to 78 years. 37% of them were smokers and 2% were alcoholics. *Heeringa et al. (2010)* study showed that current and former smoking of cigarettes was associated with increased risk of atrial fibrillation. *Frost and Vestergaard (2010)* found that consumption of alcohol was associated with an increased risk of atrial fibrillation.

As regard hypertension, 58% of our patients were hypertensive. This is consistent with *Kannel et al. (2010)* who demonstrated that hypertension conferred a 1.5- and 1.4-fold risk for men and women, respectively after adjusting for other associated conditions.

As regard diabetes mellitus, 46% of our patients were diabetic. This is

consistent with *Movahed et al. (2011)* who demonstrated DM as a strong, independent risk for the occurrence of atrial fibrillation. *Kannel et al. (2010)* demonstrated that diabetes conferred a 1.4- and 1.6-fold risk for men and women, respectively after adjusting for other associated conditions.

As regard IHD, 46% of patients had IHD. 13% of patients had COPD and as well 13% has OSA. Among the studied group 63% of patients showed no recurrence of AF while 37% showed recurrence. There was a statistically significant difference between AFCVS score value in the group with recurrent AF and group with non-recurrent AF. There was a statistically significant difference in age between patients with no AF recurrence and patients with recurrence. The recurrence group has higher age than no recurrence group in harmony with *Lee et al. (2011)* and *Ma et al. (2011).*

There was a statistically significant difference in AFCVS score value of both groups. The group with AF recurrence has a higher score. The percentage of smokers in the AF recurrence group was significantly higher than no AF recurrence group in harmony with *Kinoshita et al. (2010).* There was a significant difference between both groups regarding hypertension. Percentage of hypertensive patients was higher than non-hypertensive in the recurrence group, in harmony with *Berruezo et al. (2011).*

The value of HBA1c was significantly higher in AF recurrence group. The LVEF was significantly higher in no AF recurrence group. It was the first episode of AF in 31% of patients. Medical cardio-version was tried and failed in 56%. And it was the first time to have ECV in 74% of patients. Pharmacologic cardio-version is less effective, and time to conversion is unpredictable and may be relatively long according to *Camm et al. (2011).*

There was a statistically significant difference between no recurrence and recurrence group regarding all the parameters of the AFCVS score. Age was higher in the recurrence group. The percentage of first AF episode was higher in no AF recurrence group. The presence of cardiac failure and vascular disease was higher in the recurrence group. The positive history of a short interval from last AF episode was significantly higher in recurrence group.

A binary logistic regression was run to evaluate AFCVS score as a predictor for the recurrence among the patients in the study population. There was homoscedasticity and normality of the residuals. The binary logistic regression model was statistically significant with insignificant Hosmer and Lemeshow test. AFCVS score was a significant predictor for the AF recurrence in the studied population.

The diagnostic efficacy and cut off point of AFCVS for prediction of AF recurrence in the studied sample was determined using a receiver operating characteristic curve (ROC) and the AFCVS score cut off point was 5. The score showed 83.8% sensitivity, 68.3% Specificity, 87.8% negative predictive value, 60.8% positive predictive value and 74% accuracy.

In this study we have done another set of comparisons between cases according to the AFCVS score cut off point. The cutoff point 5 divided the cases into 2

groups: group <5 included 48 patients & group>5 included 52 patients.

The age and the presence of hypertension and IHD were significantly higher in patients with AFCVS score>5. The LVEF and level of HDL was significantly higher in patients with AFCVS score <5 *Heeringa et al. (2010).*

CONCLUSION

The risk of unsuccessful outcome of ECV can be predicted using five simple clinical variables: A-- Age. F-- Not First time AF. C-- Cardiac failure. V-- Vascular disease. S-- Short duration from previous AF (within 1 month before electrical cardio-version (ECV)). The AFCVS score has a 83.8% sensitivity and 74% accuracy.

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التنبوء بفشل الصدمات الكهربية القلبية في علاج الرجفان الأذيني (AF-CVS) عن طريق إستخدام مجموع نقاط

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خلفيـة البحـث: يبقـي مـرض الرجفـان الأذينـي واحـدا مـن أكبـر أسـباب جلطـات الـدم، وقصـور وظائف القلـب، والمـوت المفـاجئ. ويضـاعف مـرض الرجفـان الأذينـي مـن خطـورة أسـباب الوفيـات فـي السـيدات, كمـا يزيـد منهـا فـي الرجـال الـي مـرة ونصـف. ويعـوق هـذا المـرض حيـاة مرضـاه فهنـاك مـايقرب مـن 10-40% مـن مرضـي الرجفـان الأذينـي يتـرددون علـي المستشـفيات سـنويا لهـذا السـبب فقـط. وعـلاج الصـدمات الكهربيـة القلبيـة يعـد علاجـا أساسـيا فـي حـالات الرجفـان الأذينـي الحـاد ولهـذا, فـإن تعريـف الحـالات ذات القابليـة العاليـة لفشـل هـذه الصـدمات الكهربيـة أو العرضـة المبكـرة لتكـرار هـذه النوبـة مـن الرجفـان الأذينـي يبقـي ذات أهميـة كبيـرة فـي اتخاذ القرار الطبي المناسب.

الهـدف مـن البحـث: الوصـول إلـي أداة مطابقـة لتعريـف الحـالات الأكثـر عرضـة لعـدم نجاح الصدمات الكهربية القلبية في علاج حالات الرجفان الأذيني الحاد.

المرضـى وطـرق البحـث: هـذه دراسـة جماعيـة أجريـت بـين مـارس 2018 ومـارس 2019. وقـد تـم تسـجيل 100 مـريض متتـالي تـم قبـولهم فـي مستشـفي الحسـين، جامعـة الأزهـر تعرضـوا للرجفـان الأذينـي الحـاد الـذي يتطلـب إصـدارًا كهربائيًـا مباشـرًا. (نسـخة كهربائيـة DC). بعـد الحصـول علـى موافقـة مسـتنيرة مـن كـل مـريض بعـد شرح كامل لأهداف البحث والغرض من هذه الدراسة.

نتـائج البحـث: حـدث تكـرار لحالـة الرجفـان الأذينـي الحـاد فـى 37 مـريض, بينمـا 63 مـريض لـم يحـدث لهـم أى تكـرار للرجفـان الأذينـى بعـد شـهر مـن العـلاج بالصـدمات الكهربيـة. وقـد وجـدنا فارقـاً بـين مجمـوع النقـاط للحـالات التـى لـم تظهـر تكـرار للرجفـان ومجمـوع النقـاط للحـالات التـى أظهـرت تكـراراً. وكـان هـذا الفـارق ذو دلالـة احصـائية حيـث أن مجمـوع النقـاط للحـالات التـى نجـح فيهـا علاج الصـدمات الكهربية

فــى منــع تكــرار الرجفــان الاذينــى اقــل مــن مجمــوع النقــاط للحــالات التــى فشــل فيهــا العــلاج بالصــدمات الكهربيــة. وعلــي ذلــك، فــإن مجمــوع النقــاط يمكــن أن يســتخدم فــى التنبــوء بنجــاح العــلاج بالصــدمات الكهربيــة مــن عدمــه. وقــد أظهــر مجمــوع النقــاط فعاليــة تشــخيص بنســبة حساســية 84% تقريبــا, ونســبة خصوصيــة 63%, وكانــت القيمــة التنبؤيــة الإيجابيــة 61%تقريبــا, والقيمــة التنبؤيــة الســلبية 88% تقريبــا, ودقــة مجموع النقاط كانت بنسبة 74%.

الإســتنتاج: يمكــن التنبــوء بمخــاطر النتيجــة غيــر الناجحــة لتقــويم نظــم القلــب الكهربــائي باســتخدام خمســة متغيــرات ســريرية بســيطة: العمــر، المــرة الأولــى الرجفــان الأذينــي، قصــور القلــب، أمــراض الأوعيــة الدمويــة، مــدة قصــيرة مــن الرجفــان الأذينــي الســابق في غضون شهر واحد قبل إصدار القلب الكهربائي.

الكلمــات الدالــة: الصــدمات الكهربائيــة القلبيــة، الرجفــان الأذينــى الحــاد، مجمــوع نقــاط ايه اف سى فى اس.