

## Benefit of CHA<sub>2</sub>DS<sub>2</sub>-VASc Score in Predicting Implantable Cardioverter Defibrillator Shocks

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### ABSTRACT

**Introduction:** Implantable cardioverter defibrillators (ICDs) reduce the risk of sudden death in eligible patients. However, it is thought that there is a relationship between the ICD shocks and increased morbidity and mortality. In this study, we examined the relationship between ICD shocks and the CHA<sub>2</sub>DS<sub>2</sub>-VASc scoring, which has gained frequent use in predicting cardiac events recently.

**Material and Methods:** Retrospective baseline characteristics and three-year follow-ups of patients with ICDs with appropriate indication were studied. Patients were divided into two groups: patients who have received ICD shock(s) and patients who have not received any ICD shock. These groups were compared for baseline characteristics and CHA<sub>2</sub>DS<sub>2</sub>-VASc scores.

**Results:** CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of heart failure (HF) patients in our study population were significantly higher than those who did not receive any shock within three years following the ICD implantation. The rate of appropriate or inappropriate ICD shocks was %16 in the HF patients implanted with ICD for primary prevention while it was %66 in patients implanted with ICD for secondary prevention. The incidence of atrial fibrillation was 68% in 37 patients who received inappropriate shock while it was 7% in those who did not receive inappropriate shock (those who received appropriate shocks or did not receive any shock) ( $p < 0.001$ ).

**Conclusion:** In conclusion, this study demonstrated a relation between the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and appropriate and inappropriate ICD shocks. The CHA<sub>2</sub>DS<sub>2</sub>-VASc score is a simple tool that may predict ICD shocks.

### Keywords

CHA<sub>2</sub>DS<sub>2</sub>-VASc score, Implantable cardioverter defibrillators, Inappropriate shock.

### Introduction

It has been shown in several studies that implanted cardioverter defibrillators (ICDs) reduce mortality in patients with sudden cardiac arrest and high-risk heart disease [1-3]. These devices terminate the attacks of ventricular tachycardia (VT) and ventricular fibrillation (VF) via delivering an electric shock whenever necessary. Despite these beneficial effects, however, inappropriate shock remains an important side effect of ICDs. 50-

70% of patients with ICD were found to receive appropriate shock due to VT/VF within two years after implantation [4]. In the first generation ICDs, inappropriate shocks were reported to be 15-25% [5]; new generation devices were also reported to have similar inappropriate shock rates [6,7].

Even though ICDs frequently save lives, they have negative effects on the quality of life and psychological state of the patient as the number of shocks increases. It has been found that the physical and mental health of the patients deteriorate as the number of ICD shocks increases [8-13]. Besides, it leads to significantly higher health care cost as the lifespan of the devices is reduced.

Recent subanalyses of large ICD studies have shown that shocks are associated with mortality. However, whether these shocks contribute to mortality or they are more prevalent in subgroup of patients with high mortality is debated. If it is possible to determine which patients have a higher risk of shock after ICD implantation, there may be an increased chance of taking the necessary precautions to prevent these shocks.

In recent years, the CHA<sub>2</sub>DS<sub>2</sub>-VASc (congestive heart failure, hypertension, age ≥75, diabetes mellitus, previous stroke or transient ischemic attack or thromboembolism, vascular disease, age 65-74 years, sex category) score has been suggested to be able to determine mortality and morbidity in various circumstances, other than atrial fibrillation (AF) which it was initially used for [14-17]. Therefore we investigated the relationship between CHA<sub>2</sub>DS<sub>2</sub>-VASc score and appropriate/inappropriate shocks in ICD-implanted patients.

## Material and Method

### Patient population

We retrospectively studied the baseline characteristics and three-year follow-up data of the patients who were diagnosed with HF and implanted with ICD in our clinic between 2011 and 2014. The study population consisted of ICD-implanted patients due to a documented VT diagnosis or chronic heart failure (CHF) diagnosis without a documented attack, according to the current guidelines. Parameters such as baseline physical examination, risk factors, electrocardiography (ECG), and echocardiography and laboratory results were noted from the patient's files. Patients who were unable to complete the three-year follow-up period for any reason (except those who received an ICD shock due to arrhythmia and died) were removed from the study. Patients were grouped as shocked and non-shocked and the characteristics between these groups were compared. The study protocol was approved by the local ethics committee.

### The devices and programs used

All patients were implanted with ICD devices (Biotronik, Germany) through the left pectoral region. Threshold and sense measurements of the patients were performed during and after the procedure. Standard programs were used in the defibrillators. When the heart rate is within the range of 130-161 bpm (Zone 1), the device recorded the event without giving any treatment. Ventricular arrhythmias faster than 162 bpm (Zone 2) were considered as VT, and the ICD was programmed to apply antitachycardia pacing (ATP) with 2 bursts and 2 ramps initially. If the arrhythmia persisted, the device delivered a defibrillator shock. When the rate of ventricular arrhythmia was faster than 210 bpm (Zone 3), the device was programmed to deliver a shock as the first treatment. In all devices, algorithms for discrimination of supraventricular tachycardia (SVT) and VT were activated to avoid inappropriate shocks.

### Follow-up

In all patients, devices were checked every three months and recorded data were saved. Appropriate and inappropriate shocks

were identified and recorded. The shocks that were not given for VT or VF in the records were interpreted as inappropriate shock. Patients who had missing data for more than 6 months during the follow-up were considered incomplete follow up and excluded from the study.

### Statistical analysis

Shapiro-Wilk (when n<50) or Kolmogorov-Smirnov (when n>50) test was used for testing the normal distribution of numerical variables. Groups were compared using Independent Samples t-test (for normally distributed variables) or Mann-Whitney U test (for non-normally distributed variables). Differences between categorical variables were compared using Pearson Chi-Square test in 2x2 tables. Pearson Correlation Coefficient was used in the analysis of relations between numerical variables. In multivariate analysis, logistic regression analysis (backward method) was used to investigate the effect of probable factors determined in univariate analyses on the ICD shock. Statistical analyses were performed with R 3.3.2v program (open source), and the significance level was set at p<0.05.

## Results

Patients who underwent ICD implantation due to CHF were divided into two groups: (1) those who received appropriate or inappropriate shock (shocked, n = 69) and (2) those who did not receive any shock within three years (non-shocked, n = 137) after ICD implantation. The demographic characteristics of the patients were summarized in Table 1.

The mean age, female sex ratio, the rate of hypertension (HT), diabetes mellitus (DM), AF, stroke, and peripheral artery disease (PAD), and mean CHA<sub>2</sub>DS<sub>2</sub>-VASc scores were found significantly higher in the shocked group than the non-shocked group (Table 1).

	Shocked (n=69)	Non-Shocked (n=137)	p
Age, year	66.9 ± 9.1	57.4 ± 8.9	<0.001
Male gender, n (%)	39 (%57)	106 (%77)	0.002
Hypertension, n (%)	65 (%94)	61 (%45)	<0.001
Diabetes Mellitus, n (%)	48 (%70)	48 (%35)	<0.001
Dyslipidemia, n (%)	32 (%46)	55 (%40)	0.393
Smoking, n (%)	39 (%57)	96 (%70)	0.053
Ischemic etiology, n (%)	53 (%77)	106 (%77)	0.928
Primary prevention ICD recipients, n (%)	21 (%30)	112 (%82)	<0.001
Secondary prevention ICD recipients (%)	48 (%70)	25 (%18)	<0.001
History of AF, n (%)	31 (%45)	5 (%4)	<0.001
Stroke, n (%)	29 (%42)	6 (%4)	<0.001
Peripheral arterial disease, n (%)	37 (%54)	28 (%20)	<0.001
Body mass index, kg/m <sup>2</sup>	26.8 ± 2.4	27.0 ± 2.5	0.477
Systolic blood pressure, mmHg	126 ± 7.8	125 ± 7.0	0.870
Diastolic blood pressure, mmHg	74.2 ± 6.0	74.0 ± 6.2	0.804
Pulse, bpm	67.5 ± 6.4	68.3 ± 6.0	0.352
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	5.16 ± 1.45	1.98 ± 1.01	<0.001

**Table 1:** Comparison of baseline demographic and clinical features

of shocked and non-shocked patients within three years after ICD implantation.

The rate of those receiving appropriate or inappropriate ICD shocks was 16% in patients with ICDs for primary prevention whereas this rate was 66% in patients with ICDs for secondary prevention ( $p < 0.001$ ).

Patients' baseline laboratory and echocardiographic findings were summarized in Table 2.

	Shocked (n=69)	Non-Shocked (n=137)	P
Ejection fraction, %	27.4 ± 5.5	33.5 ± 3.6	<0.001
Hemoglobin, gr	12.5 ± 1.6	13.1 ± 1.5	0.016
MPV	10.9 ± 0.9	10.7 ± 0.8	0.265
WBC, x103	7,93 ± 1,82	7.79 ± 1.87	0.621
Platelet, x103	257 ± 86	256 ± 63	0.898
eGFR	57.1 ± 12.4	82.1 ± 10.9	<0.001
Na	136.1 ± 4.0	135.1 ± 10.8	0.463
Blood glucose, mg/dL	139 ± 25	111 ± 17	<0.001
Albumin, gr	3.74 ± 0.35	3.75 ± 0.29	0.795
Total cholesterol	188 ± 40	196 ± 40	0.173
LDL	117.1 ± 33.8	119.3 ± 36.8	0.674
HDL	40.4 ± 11.6	40.0 ± 10.2	0.789
Triglyceride, mg/dL	114 (84-191)	138 (97-208)	56

**Table 2:** Comparison of echocardiographic findings and laboratory values of the study groups.

MPV: Mean Platelet Volume, WBC: White Blood Cell Count, eGFR: Estimated Glomerular Filtration Rate, Na: Sodium, LDL: Low Density Lipoprotein, HDL: High Density Lipoprotein.

While 68% of the 37 patients who received inappropriate shock were in AF rhythm, AF frequency was 7% in those who did not receive inappropriate shock (appropriate shocks or no shock) ( $p < 0.001$ ) (Table 3).

	Inappropriate shock recipients (n=37)	Appropriate shock recipients + Non-shocked (n=169)	P
Atrial fibrillation, n (%)	25 (%68)	11 (%7)	<0.001

**Table 3:** Comparison of the study groups in terms of atrial fibrillation.

Logistic regression analysis revealed a significant relationship between the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and the ICD shocks (Table 4).

	RR (%95 CI)	P
HT	4.911 (1.107-21.791)	0.036
CHA <sub>2</sub> DS <sub>2</sub> -VASc score	6.263 (3.32-11.814)	<0.001
Primary prevention ICD recipients	0.186 (0.059-0.587)	0.004

**Table 4:** Logistic Regression Table.

## Discussion

In this study, factors that could predict the defibrillator shocks in patients with ICDs were investigated. In the study population, the mean CHA<sub>2</sub>DS<sub>2</sub>-VASc scores of the group receiving appropriate or inappropriate shocks were found significantly higher than those who received no shock during the three-year follow-up period after the ICD implantation.

The rate of the patients who received appropriate or inappropriate shock within the three-year follow-up period was 33%. This rate was consistent with the results of previous studies [18]. In a meta-analysis study covering ten large ICD studies (200,000 patients), Proietti et al. showed a correlation between ICD shocks and mortality. This relationship was stronger in appropriate shock recipients (HR 2.95, 95% CI 2.12-4.11,  $p < 0.001$ ). But the relationship was also statistically significant in inappropriate shock recipients (HR 1.71, 95% CI 1.45-2.02,  $p < 0.001$ ). Moreover, the combination of appropriate and inappropriate shocks was found to have greater mortality risk [19].

There are different opinions about reasons of high mortality in ICD shock recipients. Some studies have shown that myocardial damage develops after ICD shocks [20]. In some clinical studies, it was found that markers of cardiac damage were elevated after ICD shocks [21].

Some authors have associated the increased mortality with the inappropriate shocks due to AF and argued that there is an indirect relationship between these two [22]. The frequency of AF was significantly higher in shocked patients in our study too. Since AF is the most common cause of inappropriate shocks, these explanations may be accurate. It would be reasonable to assume that both the frequency of arrhythmia and the mortality also increase in patients receiving appropriate shocks as a result of worsening cardiac insufficiency. The results of our study suggest that comorbid conditions that may be reasons for poor clinical prognosis such as stroke, DM, PAD increase the shock frequency.

Recent studies have shown that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, which has been recently used as a risk scoring system for AF and stroke, also predicts mortality and morbidity in other cardiac diseases [17,23]. It has been shown that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score might be a predictor for hospital mortality in patients with HF independently of all other comorbid parameters [24]. It has also been showed that the CHA<sub>2</sub>DS<sub>2</sub> (congestive heart failure, hypertension, age  $\geq 75$ , diabetes mellitus, previous stroke or transient ischemic attack or thromboembolism) score could predict cardiovascular events in coronary artery disease patients without AF [25].

We found in our study that the CHA<sub>2</sub>DS<sub>2</sub>-VASc score was significantly higher in patients who received shock. We studied the CHA<sub>2</sub>DS<sub>2</sub>-VASc score irrespective of the shock being appropriate and inappropriate because both were associated with increased mortality and morbidity, as mentioned earlier. We found that the parameters included in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score such as HT, DM, age, female gender, and PAD were also independently associated

with shocks. From this point of view, this scoring system is expected to be associated with ICD shocks.

In our study, eGFR levels, a marker of renal function, were found to be lower in the patients who received ICD shock, independent of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score. This finding suggests that kidney disease poses a risk for ICD shocks. In line with this, a new score was recently developed to include the kidney disease in the risk score [26].

In our study, ICD shocks were more frequently observed in patients who were had ICD implanted for secondary prevention. This finding was expected as it has been confirmed in several previous studies [27].

We did not find a relationship between smoking and ICD shocks in our study. However, Sanchez et al. found a significant relationship between smoking and ICD shocks in a previous study [28].

### Conclusion

In conclusion, we found a correlation between the CHA<sub>2</sub>DS<sub>2</sub>-VASc score and ICD shocks. This may allow prediction, prevention, or reduction of ICD shocks. For this purpose, the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, as a simple, easy to calculate, and objective scoring system, may be useful for this purpose. Prospective randomized trials may provide more definitive results in this subject.

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