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Research Article

Increased Dispersion of Atrial Refractoriness Predicts Most of the Inappropriate Implantable Cardioverter-Defibrillator Shocks

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Keywords

- Implantable Cardioverter-Defibrillators
- Inappropriate Shocks
- Atrial Refractoriness

Abstract

Background: Despite implantable cardioverter-defibrillators' proven survival benefits, inappropriate shocks limit their benefits due to adverse effects on quality of life, potential arrhythmogenesis, and even mortality. Atrial fibrillation (AF) is the most common cause of inappropriate shocks. Therefore, to predict and treat AF may prevent inappropriate shocks and their hazardous potentials. This paper aimed to show that we could predict the patients who may experience inappropriate implantable cardioverter-defibrillator shocks by measuring atrial refractoriness.

Methods: 186 consecutive patients who underwent initial ICD implantation underwent coronary angiography and electrophysiologic (EP) study before the ICD implantation.

Results: Of 169 patients who could be followed, 34 received (20%) at least one inappropriate shock during the mean follow-up of 30 months. The majority of these shocks were due to AF (68%). The most significant predictors for these inappropriate shocks were atrial effective refractory periods (AERPs) and AERP dispersion.

Conclusions: We found that simple EP study parameters measuring atrial refractoriness may define the patients carrying higher risk for future inappropriate shocks due to AF. We could prevent inappropriate shocks and hazardous results in these patients by either device programming, pharmacological treatments, or ablation procedures.

INTRODUCTION

Although implantable cardioverter-defibrillator (ICD) therapy is proven to reduce mortality[1], inappropriate shocks result in several adverse effects, including impaired quality of life [2], ventricular arrhythmias [3], and even may increase mortality [4]. The incidence of inappropriate shock in patients implanted with an ICD ranges from %10 to 44 [5-10]. Several studies showed that atrial fibrillation (AF) is the most common reason for inappropriate ICD therapy [4,6, 9-11] and increases the risk of an inappropriate shock by 3-folds [7]. Therefore, predicting and treating AF in these patients may prevent more than half of the inappropriate shocks and their adverse effects. Atrial effective refractory period (AERP) has been used as a parameter to evaluate atrial repolarization, and AERP and its dispersion are known parameters of atrial vulnerability that indicate enhanced atrial arrhythmogenesis [12,13]. We aimed to predict patients with inappropriate ICD shocks due to AF by using atrial refractory parameters.

METHODS

We performed a prospective study that enrolled 186 consecutive patients who underwent initial ICD implantation in our clinics between 2012-2016 years. Written informed consent was obtained from all patients, and the local ethics committee approved the study. The patients enrolled in this study underwent coronary angiography to define the need for revascularization and electro physiologic (EP) study before the ICD implantation. The patients who needed any revascularization procedure, the patients with a history of AF were excluded. We implanted ICD in all the patients in the study either on the same day or the day after the EP study. Transthoracic echocardiography was performed in all patients before the procedures. In general, device programming was as follows. The ventricular fibrillation (VF) zone detected ventricular events faster than 185-200 beats/min, and initial therapy was 30 J or more. Ventricular tachycardia zone detected ventricular events faster than 160-170 beats/min, and three sequences of ATP were initially attempted. If arrhythmia continued, the first shock with an energy ranging 10-20 J and subsequent shocks with maximal energy were delivered till its termination. The device-related detection algorithms were employed for the discrimination of supraventricular tachycardia [4, 14]. All the patients were followed in our outpatient ICD clinic. Any ICD therapy not delivered for VT or VF was deemed

inappropriate, and the rhythm triggering therapy was categorized as atrial fibrillation or flutter (AF), other supraventricular including sinus tachycardia (SVT), or inappropriate sensing using published criteria [15].

Electro physiologic Study: Baseline EP study was performed in all patients in a fasting and unsedated state. Two multipolar electrode catheters were inserted through femoral veins and placed in the high right atrium (HRA) and lower right posterolateral atrium (RPL). One steerable decapolar catheter was inserted into the coronary sinus (CS) in the same way. Intra cardiac electro grams were displayed simultaneously with ECG leads I, II, and V1 on a multichannel oscilloscope recorder. For the EP study, the PA interval was defined as an interval from the onset of earliest atrial activation on the surface ECG to the rapid deflection of the atrial ECG at the His-bundle site. This interval was used as a scale of right atrial conduction. AERPs in the HRA, RPL, and distal CS were assessed just we described before [13]. AERP dispersion was defined as a maximal difference of AERPs at the three stimulation sites.

Statistical Analysis

Continuous variables are expressed as mean±SD and categorical variables as percentages. The two-tailed unpaired t-test for independent variables was used for the analysis of continuous variables. Chi-square or Fisher's exact test assessed differences in categorical variables of two groups. Univariate and multivariate logistic regression analysis was used to assess the relation of variables with inappropriate ICD shocks. Odds ratios and 95% confidence intervals were listed. A p-value <0.05 was considered statistically significant. A receiver operating characteristic curve evaluated the sensitivities and specificities at different cut points of some AERP parameters.

RESULTS

One hundred eighty-six patients enrolled in this study initially, but we could follow up 169 patients. Of 169 patients, 34 received (20%) at least one inappropriate shock during the mean follow-up of 30 months. However, 24 of these shocks were due to AF (71%), followed by supraventricular tachycardias, including sinus tachycardia (21%) and abnormal sensing (8 %). The age, sex, left ventricular ejection fraction (EF), NYHA class, ICD indication, underlying heart diseases, left atrial diameters, serum creatinine levels, diabetes mellitus, hypertension, pharmacological therapy, QRS durations were comparable between the two groups (Table 1).

The patients with inappropriate shocks due to AF had significantly higher PA intervals and AERP dispersions but lower AERP at HRA, RPL, and DCS (Table 2).

Regression analysis showed that left atrial diameter, PA interval, AERP at HRA and RPL, and AERP dispersion were independent variables predicting the inappropriate shocks (Table 3). $AERP_{HRA}$ >190 msec separated the patients with inappropriate shocks from those without with a sensitivity of 68% and a specificity of 98%. AERP dispersion >60 msec separated the patients with inappropriate shocks due to AF with a sensitivity of 92% and specificity of 98%.

Table 1. Baseline patient characteristics.

Variables	Inappropriate shocks due to AF (p=24)	No inappropriate shocks (p=135)	p
Age (year)	59.4±12.8	61.6±13.1	NS
Sex (male)	17	89	NS
Diabetes Mellitus (n)	7	35	NS
Hypertension (n)	17	80	NS
Current smoker (n)	3	13	NS
QRS duration >0.12 sec (n)	5	33	NS
Left Ventricular Ejection Fraction (%)	27.4±5.5	28.2±5.3	NS
Left atrial diameter (cm)	4.3±1.1	4.3±0.9	NS
NYHA Class (%) II III	 35 65	 35 65	NS
Serum creatinine (mg/dl)	1.16±0.55	1.18±0.52	NS
Primary prevention (n)	20	111	NS
Etiology (%) Ischemic Non-ischemic	 60 40	 63 37	NS
Device type (n) Single chamber Dual Chamber CRT	 14 4 6	 90 15 30	NS
Pharmacological therapy (%) Beta-blocker Amiodarone ACEI/ARB Digitalis Aldosterone antagonist Nitrate Statin Ivabradine Furosemide	 70 7 60 15 55 25 20 15 85	 72 6 64 14 53 23 19 14 85	 NS NS NS NS NS NS NS NS NS

Table 2. Electro physiologic Parameters of Patients with and without Inappropriate Shocks

Variables	Inappropriate shocks (p=34)	No inappropriate shocks (p=135)	p-value
PA interval (msec)	34.7±9.3	22.5±6.0	0.001
$AERP_{HRA}$ (msec)	195.3±16.3	223.9±14.2	0.001
$AERP_{RPL}$ (msec)	183.8±19.3	223.3±14.7	0.001
$AERP_{DCS}$ (msec)	189.7±19.7	232.3±14.7	0.001
AERP dispersion (msec)	74.4±10.3	45.9±8.4	0.001

AERP: Atrial Effective Refractory Period, DCS: Distal Coronary Sinus, HRA: High Right Atrium, RPL: Right Posterolateral Atrium

Table 3. Predictors of ≥ 1 inappropriate shocks

Variables	B	S.E.	t	p-value
LA	-0.08	0.01	-2.0	0.04
PA	0.2	0.002	3.8	0.0001
$AERP_{HRA}$	0.6	0.002	6.1	0.0001
$AERP_{RPL}$	-1.0	0.005	-3.4	0.001
AERP dispersion	0.4	0.0001	8.8	0.0001

DISCUSSION

Atrial electrical remodeling plays a part in the occurrence of AF. An increase in heterogeneity of atrial refractoriness

may facilitate the occurrence of multiple reentry wavelets and vulnerability to AF [16,17]. Recently, Lee et al. [18] showed that tissue refractoriness to conduction is a crucial electrophysiological factor in determining susceptibility to fibrillation. In patients with no overt structural heart diseases, AERP of ≥280 msec was predictive of an increased future risk of developing AF. Moreover, we know that atrial remodeling due to congestive heart failure (CHF) is characterized by structural changes, conduction abnormalities, sinus node dysfunction, and increased refractoriness. These abnormalities may partly be responsible for the increased propensity of AF in these patients [19]. Since AF is the most common cause of inappropriate shocks [4,6,7,9-11], it is reasonable that increased atrial refractoriness may predict the AF development and inappropriate shocks in these patients.

Large-scale studies have estimated the incidence of inappropriate shock in patients implanted with an ICD to range from 10% to 44% [5-10]. Similarly, of 169 patients, 34 received (20%) at least one inappropriate shock in our study. The most common cause of inappropriate shocks is AF [4, 6, 9-11], and AF increases the risk of an inappropriate shock by 3-folds [7]. Similar to our results (24 of these shocks were due to AF (71%)), Yang JH et al. [20] found that 67.7 % of inappropriate shocks are due to AF. It is clear that inappropriate shocks reduce the quality of life due to pain and psychological morbidity [2], may induce ventricular arrhythmias [3], and even may increase mortality [4,9]. Therefore, patients at increased risk for inappropriate shocks need careful evaluation of potential therapeutic optimization strategies, including pharmacological treatment, device programming, electrophysiological ablation.

For inappropriate shocks, several independent predictors are defined before, including most commonly prior AF, smoking, HT, younger age, absence of diuretics, NYHA class, etiology, and device type [4-8, 10, 21-23]. In our results, age, sex, left ventricular ejection fraction (EF), NYHA class, ICD indication, underlying heart diseases, left atrial diameters, serum creatinine levels, diabetes mellitus, hypertension, pharmacological therapy were similar in the two groups. However, more remarkable results were in atrial refractory periods. The patients with inappropriate shocks due to AF had significantly higher PA intervals and AERP dispersions but lower AERP at HRA, RPL, and DCS. Inappropriate shocks due to AF were related to increases in LA diameter, PA interval, and AERP dispersion and decreases in $AERP_{HRA}$, $AERP_{RPL}$, $AERP_{DCS}$. Age, left ventricular ejection fraction, device type, and other clinical parameters were not significantly related to inappropriate therapy due to AF. An AERP dispersion> 60 msec increased the risk of AF causing inappropriate shocks by 3.8 folds (p=0.001, 95% CI: 1.5-8.8).

CONCLUSION

As a result, simple EP study parameters measuring atrial refractoriness may define patients with a higher risk for future inappropriate shocks due to AF. We could prevent inappropriate shocks and hazardous results in these patients by either device programming, pharmacological treatments, or ablation procedures.

DECLARATIONS

We would like to submit the manuscript entitled ' Increased Dispersion of Atrial Refractoriness Predicts Most of The Inappropriate Implantable Cardioverter Defibrillator Shocks' for publication in your journal.

This manuscript is not published before and not under consideration in another journal. Availability of data and material Data and materials are available from the corresponding author on reasonable request.

Approval of the research protocol

Ethics approval and consent to participate We informed the participants about the study and got consent written informed consent from the participants.

This study was approved by the Ethics Board of the Institutional Ethics Committee of Lokman Hekim University.

Informed consent: Yes

Author's contributions OO contributed design of the work, analysis, interpretation of data, have drafted the work and substantively revised it. OY contributed analysis. HA contributed interpretation of data and substantively revised it. All authors have read and approved the manuscript.

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