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Predictors of sinus rhythm return during defibrillation testing in patients with permanent atrial fibrillation undergoing implantation of a cardioverter-defibrillator

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Abstract

Background: Atrial fibrillation (AF) is present in a significant proportion of patients treated with an implantable cardioverter-defibrillator (ICD). Defibrillation testing may lead to sinus rhythm (SR) restoration which may be hazardous due to the increased risk of thromboembolic complications in these patients.

Aim: To identify predictors of SR restoration during defibrillation testing in patients with permanent AF undergoing ICD implantation.

Methods: Permanent AF was present in 79 (12%) of 671 consecutive patients who received ICD in our institution between 2005 and 2010. In this group, 47 patients (mean age 64 ± 12 years, 38 males) underwent defibrillation testing during the implantation procedure and in the remaining 32 patients defibrillation testing was not performed due to various contraindications. Sinus rhythm was restored in 17 (36%) patients, while AF was still present after defibrillation testing in the remaining 30 patients. We analysed demographic, clinical, echocardiographic and electrophysiological parameters which could identify those patients in whom SR was restored, using univariate and multivariate analysis as well as constructing ROC curves.

Results: Demographic parameters and clinical history were similar in both groups. Patients in whom SR was restored had smaller left atrial diameter (49.9 ± 5.9 *vs* 59.4 ± 6.1 mm, $p < 0.001$), more often received a double-coil defibrillation lead (83% *vs* 10%, $p < 0.001$), had less advanced heart failure as assessed using NYHA classification ($p < 0.05$), and were more frequently treated with amiodarone (47% *vs* 23%, $p < 0.025$). The chance of SR return was increased 11 times in patients receiving amiodarone, 6 times in patients with a double-coil lead, 2 times in patients with lower NYHA class, and 1.36 times in patients with smaller left atrium diameter (for each 1 mm increase). The ROC curves showed that using the cut-off value for the left atrial diameter of 47 mm, patients prone to SR restoration were identified with a sensitivity of 65%, specificity of 100%, positive predictive value of 83%, and negative predictive value of 90% (area under curve 0.904, 95% CI 0.809–1.0). Multivariate analysis showed that NYHA class, amiodarone usage, type of defibrillating lead and left atrial diameter were independent predictors of SR restoration.

Conclusions: Atrial fibrillation was present in 12% of consecutive patients undergoing ICD implantation and was terminated by defibrillation testing in 36% of those who underwent this test. The NYHA class, amiodarone usage, type of defibrillating lead and left atrial diameter were independent predictors of SR restoration.

Key words: defibrillation testing, atrial fibrillation, sinus rhythm restoration

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INTRODUCTION

The goal of treatment with an implantable cardioverter-defibrillator (ICD) is to prevent sudden cardiac death due to ventricular fibrillation (VF) and thus testing the effectiveness of defibrillation is an important component of the intraoperative patient evaluation. All procedural aspects, including lead choice, location, type, and ICD programming must serve the main purpose of providing the most effective defibrillation capability [1–7]. Effectiveness of defibrillation is tested during or after ICD implantation, with the goal being VF termination using an energy impulse with a safety margin > 10 J below the maximal energy output of the ICD device [7].

Atrial fibrillation (AF) is present in 9–16% patients treated with ICD due to malignant ventricular arrhythmia [1, 3, 4, 6–9]. The presence of AF poses problems including the need of differentiation between atrial and ventricular arrhythmia. Atrial fibrillation may be inappropriately detected by ICD as VF and/or ventricular tachycardia, leading to activation of the ventricular defibrillation programme.

In patients with apparently permanent AF, VF defibrillation may result in an unexpected SR restoration. This is a clinically important issue as patients with AF usually require long-term anticoagulation unless long-term SR maintenance, present in up to 20% patients during 1 year follow-up, is reliably proven. Frequently, anticoagulation is stopped during perioperative period and therefore the risk of thrombo-embolic complication fallowing SR restoration is not negligible. In some cases, transoesophageal echocardiography should be considered to search for the presence of intraatrial thrombus [1, 3, 4, 6–13].

The aim of our retrospective study was to identify predictors of SR return during defibrillation testing in patients with permanent AF undergoing ICD implantation.

METHODS

We retrospectively analysed medical documentation (operative protocols and case records) of 671 patients (170 women, and 501 men, mean age 62.3 ± 12.6 years, range 17–93 years) who underwent first ICD implantation in 2005–2010. Permanent AF lasting for more than 2 years (mean 5.6 ± 3.6 years) was noted in 79 patients. A single chamber ICD was implanted in all these patients. Defibrillation testing was not performed during ICD implantation in 32 of these patients due to unavailable anaesthesiologist in 6 cases, suspected intracardiac thrombus in 3 cases, poor general condition in 6 cases, lack of anticoagulant therapy in 9 cases, and low left ventricular ejection fraction (LVEF < 15%) in 8 cases. In the remaining 47 patients (9 women, 38 men, mean age 63.9 ± ± 12.4 years), defibrillation of induced VF was performed during ICD implantation to evaluate the safety margin of the energy impulse. These patients were older than patients without AF ($p < 0.05$). They were then divided into two groups. Group SR (+) (17 patients, including 3 women) consisted of patients with SR return during ICD testing, and group SR (–) (30 patients, including 6 women) consisted of patients in whom AF persisted after ICD testing. Mean duration of AF was similar in both groups. Patient characteristics in regard to main cardiac diagnoses and comorbidities, indications for ICD implantation and drug therapy are shown in Table 1.

In the current study, we used operative protocols, case records, and the database of our information system called Impuls. We analysed the following clinical parameters: (1) indications for ICD implantation, (2) concomitant major cardiac disease and other comorbidities, (3) antiplatelet and anticoagulant therapy (acetylsalicylic acid, clopidogrel, ticlopidine, acenocoumarol, warfarin, heparin), (4) use of beta-blockers, ACE inhibitors, and diuretics, (5) antiarrhythmic therapy (amiodarone, sotalol and other drugs), (6) NYHA class, (7) body mass index (BMI), (8) LVEF measured in two echocardiographic views, and (9) anteroposterior left atrial (LA) dimension measured in the parasternal view.

We also analysed electrophysiological parameters, such as lead type (double-coil *vs* single-coil), vein used for ICD implantation (subclavian, cephalic, other), duration of the procedure, ventricular potential amplitude, pacing threshold (impulse amplitude, impulse duration, current), defibrillation energy, and ECG recordings showing SR return or AF maintenance, including surface limb ECG and intracardiac ECG recordings by ICD.

We did not measure the exact defibrillation threshold, or the lowest energy to defibrillate VF. We only evaluated the effectiveness of defibrillation, i.e. tested for the presence of adequate safety margin of the energy impulse terminating VF. We used defibrillation impulses of 10 J and 20 J (Table 1).

Statistical analysis

The results are shown as mean values ± SD with 95% CI for normally distributed data or median values with upper and lower quintiles for non-normally distributed ordinal variables. To verify hypotheses related to the purpose of the current study we used the Student t test, χ^2 test, and the Mann-Whitney U test. Correlations were evaluated using the Pearson correlation coefficient. To determine cut-off values for quantitative parameters characteristic for SR restoration, we plotted respective ROC curves. Results are shown as areas under curve (AUC), sensitivity and specificity with 95% CI, and p values. Variables that were significant in the univariate analysis were then included in the multivariate analysis. We used the logit model for a dichotomous response according to the Akaike informative criterion. Significance of the parameters of the optimal model was tested using the Wald test. The NYHA class was aggregated to two levels (class II *vs* class III and IV). Without aggregation, more than one odds ratio should be given, with comparisons of odds ratios for all possible combinations of the NYHA class (II *vs* III, II *vs* IV, III *vs* IV). A p value < 0.05 was considered statistically significant. All analyses were performed using STATISTICA version 8.0 (StatSoft, Inc. 2007), MedCalc version 10.4.3.0, and Excel (MS Office) software.

Table 1. Comparison of characteristics of patients with [SR (+)] or without [SR (–)] sinus rhythm return

Parameter	Group SR (+) (14 M, 3 W)	Group SR (–) (28 M, 2 W)	P
Age [years]	64.2 ± 12.3 (39–85)	63.5 ± 12.7 (30–82)	NS
Indications for ICD implantation:			NS
Primary prevention	10 (58.8%)	18 (60%)	
Secondary prevention	7 (41.2%)	12 (40%)	
Diseases:			NS
Previous MI	8 (47.1%)	13 (43.3%)	
Heart failure	6 (35.3%)	12 (40%)	
Valvular heart disease		4 (13.3%)	
Renal failure	3 (17.6%)	1 (3.33%)	
Hypertension	13 (76.5%)	17 (56.7%)	
No hypertension	4 (23.5%)	13 (43.3%)	
Diabetes	5 (29.4%)	8 (26.7%)	
No diabetes	12 (70.6%)	22 (73.3%)	
Obesity	6 (35.3%)	11 (36.7%)	
No obesity	11 (64.7%)	19 (63.3%)	
Body mass index [kg/m^2]	26.5 ± 6.8 (15–42.6)	26.0 ± 3.4 (21–34)	NS
NYHA class:			< 0.05
II	10 (58.8%)	7 (23.3%)	
III	7 (41.2%)	19 (63.3%)	
IV		4 (13.3%)	
LVEF [%]	25.5 ± 5.2 (20–35)	29.8 ± 12.4 (10–63)	NS
Left atrial dimension [mm]	47.9 ± 5.9 (40–61)	59.4 ± 6.1 (50–73)	< 0.001
ICD lead type:			< 0.001
Single-coil	3 (17.6%)	27 (90%)	
Double-coil	14 (82.4%)	3 (10%)	
Implantation route:			NS
Subclavian	11 (64.7%)	16 (53.3%)	
Cephalic	3 (17.6%)	4 (13.3%)	
Other	3 (17.6%)	10 (33.3%)	
Duration of the procedure [min]	70.5 ± 16.5 (45–110)	62.9 ± 18.7 (10–95)	NS
AF duration [years]	5.8 ± 3.7 (2–16)	5.5 ± 3.5 (2–15)	NS
R wave amplitude [mV]	10.5 ± 6.1 (5.5–30)	11.7 ± 5.7 (3.8–30)	NS
Slew rate [V/s]	3.40 ± 3.40 (1.1–16)	2.70 ± 1.0 (0.8–4)	NS
Pacing threshold: voltage [V]	0.65 ± 0.27 (2–1.3)	0.59 ± 0.25 (0.2–1.3)	NS
Pacing threshold: impulse width [ms]	0.54 ± 0.13 (0.5–1.0)	0.47 ± 0.09 (0.1–0.5)	NS
Pacing threshold: current [mA]	5.20 ± 5.80 (0.9–16)	3.40 ± 5.30 (0.5–22)	NS
Defibrillation energy [J]	18.00 ± 3.68 (10–20)	16.70 ± 5.77 (10–35)	NS
Drug therapy of heart failure:			NS
ACE inhibitor	17 (100%)	30 (100%)	
Beta-blocker	17 (100%)	30 (100%)	
Diuretic	10 (58.8%)	18 (60%)	
Anticoagulant therapy:			NS
Acenocoumarol/warfarin	15 (88.2%)	27 (90%)	
Acenocoumarol + ticlopidine	1 (5.9%)	1 (3.33%)	
Heparin	1 (5.9%)	2 (6.67%)	
No treatment	0 (0%)	0 (0%)	
Antiplatelet therapy:			NS
ASA	3 (17.6%)	6 (20%)	
ASA + clopidogrel	1 (5.9%)	1 (3.33%)	
ASA + ticlopidine		1 (3.33%)	
No treatment	13 (76.5%)	22 (73.3%)	
Antiarrhythmic therapy:			< 0.025
Amiodarone	8 (47.1%)	7 (23.3%)	
Other (sotalol)	4 (23.5%)	3 (10%)	
No treatment	5 (29.4%)	20 (66.7%)	

ICD — implantable cardioverter-defibrillator; MI — myocardial infarction; LVEF — left ventricular ejection fraction; AF — atrial fibrillation; ACE — angiotensin converting enzyme; ASA — acetylsalicylic acid

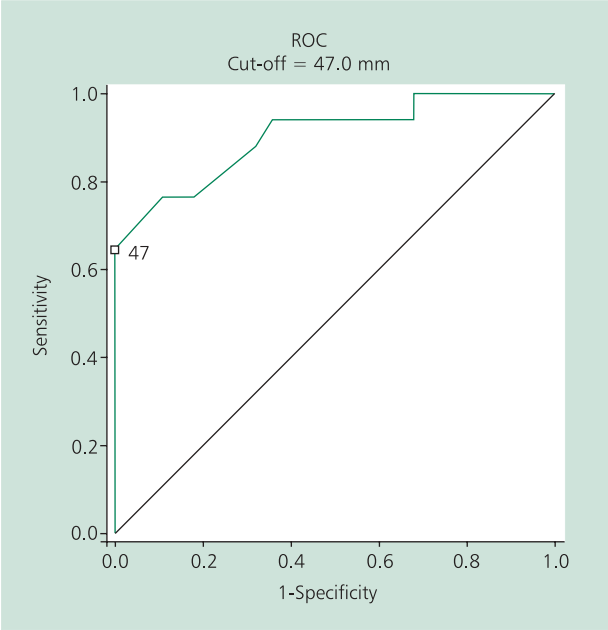

Figure 1. The ROC curve and the cut-off point for the left atrial dimension

RESULTS

Age, AF duration, distribution of major cardiac diagnoses and concomitant disease, indications for ICD implantation, drug therapy, and electrophysiological parameters except for the type of ICD lead did not differ significantly between the groups (Table 1).

The clinical characteristics of patients in the group SR (+) differed significantly from the group SR (–) only in regard to four parameters: patients in the group SR (+) had lower NYHA class and smaller LA dimension, more often had double-coil ICD lead and received more intense antiarrhythmic therapy (Table 1). We plotted a ROC curve for the LA dimension (Fig. 1), and its characteristics is shown in Table 2.

The chance of SR return was increased 11 times in patients receiving amiodarone compared to patients who were not treated with amiodarone, 6 times in patients with a double-coil lead compared to a single-coil lead, 2 times in patients with NYHA class II compared to class III–IV, and 1.36 times with each increase of the LA dimension by 1 mm (Table 3).

In the multivariate analysis, predictors of SR return included NYHA class, amiodarone treatment, the type of ICD lead, and the LA dimension.

Table 2. The ROC curve characteristics, area under curve and the cut-off point for the left atrial dimension

LA dimension cut-off value [mm]	47
Sensitivity	0.647
Specificity	1.0
Positive predictive value	1.0
Negative predictive value	0.824
Area under the ROC curve (AUC)	0.904
95% confidence interval	0.809–1.0

LA — left atrium

DISCUSSION

Evaluation of proper ICD functioning is necessary during the implantation procedure. The ICD testing is safe if contraindications are taken into account. There are two methods to test proper ICD functioning. One is to evaluate the lowest energy impulse resulting in VF termination, i.e. defibrillation threshold. Another, simpler method is to evaluate only the presence of a safe margin of energy impulse resulting in effective defibrillation of VF [3, 7, 14–16]. We used the latter method.

Sinus rhythm return during defibrillation testing may predispose to thromboembolic complications. Thus, defining clinical predictors of AF conversion to SR during defibrillation testing might guide decisions to defer such testing until adequate anticoagulation is instituted. Atrial fibrillation without effective anticoagulation is a contraindication to defibrillation testing. In our study, the presence of AF was noted in 12% of patients, and SR return was seen in 36% patients who underwent VF defibrillation during ICD implantation. These data show how common is an inadvertent SR return during defibrillation testing.

It has been shown that independent predictors of successful SR return include short AF duration, occurrence of atrial flutter episodes, and young patient age. Adverse prognostic factors include LA enlargement and coexisting organic heart disease [8–10]. Mean AF duration in our patients was 2 years and neither this variable nor age, comorbidities, drug therapy for heart failure, antithrombotic treatment and other electrophysiological parameters identified patients in whom SR returned during defibrillation testing. Our analysis showed that a major factor was LA dimension, with significantly increased chance of SR return with every reduction of LA dimension by 1 mm in the univariate analysis. Similarly, less severe heart failure as in-

Table 3. Parameters that increased the likelihood of sinus rhythm return in the univariate analysis

	Odds ratio	95% confidence interval	P
Double-coil ICD lead	6.24	2.63÷19.39	< 0.001
NYHA class	2.29	1.18÷4.43	0.014
Left atrial dimension	1.36	1.15÷1.62	< 0.001
Amiodarone therapy	10.77	1.61÷72.22	0.013

dicated by lower NYHA class also predisposed to AF conversion to SR during VF defibrillation. Unfortunately, due to a retrospective nature of our study, we were not able to analyse other echocardiographic parameters such as dimensions and wall thickness of other cardiac chambers.

In our study, amiodarone use was associated with a greater likelihood of SR return. Many studies showed that this drug is more effective in converting AF to SF compared to other drugs, and our findings are consistent with these data [6, 8, 9]

Similarly to other authors [1, 4, 5], we found that the use of double-coil ICD lead predisposes to SR return. Probably location of the second coil in the immediate vicinity of the atrium may help concentrate energy in this area. It is also possible that the use of a double-coil lead reduces defibrillation resistance, resulting in an increased defibrillation current.

Conversion of AF to SR during defibrillation of VF by ICD has been reported in the literature [1, 4, 5]. This results in a new situation. Firstly, it might be difficult to diagnose SR return in patients with VVI pacing. Surface and intracardiac ECGs in patients in patients with a slow intrinsic rhythm are dominated by paced beats. Other significant problems include potential adverse haemodynamic effects of the right ventricular apex pacing and pacemaker syndrome. Upon SR return, it may turn out that the patient actually has indications for a two-chamber and not a single-chamber ICD. What should be done in such a situation? Defibrillator change would require removal of the initially implanted device which is economically disadvantageous. However, if SR remains and patient reports adverse clinical symptoms of ventricular pacing, upgrade to a dual-chamber ICD should be seriously considered [7]. Such an approach is currently used in our centre, and in patients with a significant predisposition to SR return and maintenance we opt for an "a priori" implantation of a dual-chamber device, attempting to insert the defibrillating lead into the right ventricular outflow tract.

Finally, potential embolic complications should be borne in mind. Such patients should be given long-term anticoagulation. In our centre, acenocoumarol or warfarine is stopped 2–3 or 5 days, respectively, before the scheduled procedure and bridge subcutaneous low molecular heparin treatment is initiated (with enoxaparin 1 mg/kg given in the morning). The ICD implantation is performed when the international normalised ratio of the prothrombin time falls below 1.7. No anticoagulants are given on the day of the procedure. Acenocoumarol or warfarin is started again 12 hours after the procedure. This approach is consistent with the recommendations of the American College of Chest Physicians [3, 7, 13]. To date, we did not see any thromboembolic complications or significant bleeding in our patients.

Limitations of the study

Due to a small study sample, we could not analyse interactions between predictors of SR return. In addition, due to a retrospective nature of the study and the lack of complete data, we did not evaluate other echocardiographic parameters.

CONCLUSIONS

1. Permanent AF was noted in 12% of our patients undergoing ICD implantation, and SR return following defibrillation to terminate VF during testing after ICD implantation was seen in 36% of patients who underwent this test.
2. Sinus rhythm return was related to the type of ICD lead, antiarrhythmic therapy, LA dimension, and NYHA class.

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Czynniki wpływające na powrót rytmu zatokowego u chorych z utrwalonym migotaniem przedsionków podczas oznaczania progu defibrylacji przy wszczepieniu kardiowertera-defibrylatora serca

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Streszczenie

Wstęp: Wśród pacjentów poddawanych zabiegowi implantacji kardiowertera-defibrylatora (ICD) są także chorzy z utrwalonym migotaniem przedsionków (AF). U tych osób istnieje możliwość niespodziewanego powrotu rytmu zatokowego (SR) podczas testu defibrylacji migotania komór (VF) wykonywanego w czasie wszczepiania ICD.

Cel: Celem pracy była identyfikacja czynników determinujących powrót SR w czasie testu defibrylacji VF u chorych z utrwalonym AF poddanych wszczepieniu ICD w ramach prewencji wtórnej lub pierwotnej nagłego zgonu sercowego.

Metody: W grupie 671 chorych (śr. wieku 62,3 roku, 501 mężczyzn) poddanych implantacji ICD u 79 (12%) osób rozpoznano utrwalone AF. W tej grupie u 47 pacjentów (śr. wieku 63,9 roku, 38 mężczyzn) wykonano test defibrylacji VF przy wszczepieniu ICD, natomiast u pozostałych 32 odstąpiono od wykonania tego testu z powodu przeciwwskazań. Podczas testu u 17 (36%) pacjentów (grupa A, śr. wieku 64,2 roku, 14 mężczyzn) stwierdzono powrót SR, a u pozostałych 30 chorych (grupa B, śr. wieku 63,5 roku, 24 mężczyzn) nadal rejestrowano AF. Obie grupy porównano pod względem wskazań i technicznych szczegółów implantacji, a także danych klinicznych echokardiograficznych, stosowanego leczenia i parametrów elektrofizjologicznych. Przeprowadzono analizę jednoczynnikową i wieloczynnikową w celu ustalenia, które parametry były niezależnie związane z powrotem SR oraz wykreślono krzywe ROC dla tych zmiennych.

Wyniki: Wiek, czas trwania AF, rozkład głównych kardiologicznych schorzeń i towarzyszących chorób, wskazań do ICD, stosowanych leków (beta-adrenolityków, inhibitorów ACE, diuretyków, antykoagulacyjnych, antyagregacyjnych) oraz wartości parametrów elektrofizjologicznych (elektrycznych) nie różniły się znacząco między grupami A i B. U chorych z grupy A zarejestrowano istotnie niższe klasy niewydolności serca wg NYHA ($p < 0,05$), mniejszy wymiar lewego przedsionka ($p < 0.001$), częstsze stosowanie elektrody dwupierścieniowej ($p < 0.001$) oraz częstsze podawanie amiodaronu ($p < 0.025$). Szansa odzyskania SR przez osoby leczone amiodaronem była 10,77-krotnie większa niż przez osoby nieleczone, a przy stosowaniu elektrody dwukoilowej — 6,24-krotnie większa niż w przypadku elektrody jednokoilowej. Zmniejszenie klasy NYHA z III lub IV do II zwiększało szansę odzyskania SR 2,29-krotnie. Mniejszy o 1 jednostkę (1 mm) wymiar lewego przedsionka powodował zwiększenie szansy odzyskania SR 1,36-krotnie. W krzywej ROC optymalny punkt odcięcia dla wymiaru lewego przedsionka w celu identyfikacji chorych, u których AF ustąpiło podczas defibrylacji, wyniósł 47 mm.

Wnioski: Wśród osób z ICD utrwalone AF stwierdzono u 12% chorych i u 36% z nich po teście defibrylacji obserwowano powrót SR. Czynnikami sprzyjającymi ustąpieniu AF były konfiguracja spiral elektrody defibrylującej, mniejszy wymiar lewego przedsionka, niższa klasa NYHA oraz stosowanie amiodaronu.

Słowa kluczowe: powrót rytmu zatokowego, test defibrylacji, migotanie przedsionków

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