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Significant impact of electrical storm on mortality in patients with structural heart disease and an implantable cardiac defibrillator☆

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ABSTRACT

Background: Electrical storm (E-Storm), defined as multiple episodes of ventricular arrhythmias within a short period of time, is an important clinical problem in patients with an implantable cardiac defibrillator (ICD) including cardiac resynchronization therapy devices capable of defibrillation. The detailed clinical aspects of E-Storm in large populations especially for non-ischemic dilated cardiomyopathy (DCM), however, remain unclear.
Objective: This study was performed to elucidate the detailed clinical aspects of E-Storm, such as its predictors and prevalence among patients with structural heart disease including DCM.
Methods: We analyzed the data of the Nippon Storm Study, which was a prospective observational study involving 1570 patients enrolled from 48 ICD centers. For the purpose of this study, we evaluated 1274 patients with structural heart disease, including 482 (38%) patients with ischemic heart disease (IHD) and 342 (27%) patients with DCM.
Results: During a median follow-up of 28 months (interquartile range: 23 to 33 months), E-Storm occurred in 84 (6.6%) patients. The incidence of E-Storm was not significantly different between patients with IHD and patients with DCM (log-rank $p = 0.52$). Proportional hazard regression analyses showed that ICD implantation for secondary prevention of sudden cardiac death ($p = 0.0001$) and QRS width ($p = 0.015$) were the independent risk factors for E-storm. In a comparison between patients with and without E-Storm, survival curves after adjustment for clinical characteristics showed a significant difference in mortality.
Conclusion: E-Storm was associated with subsequent mortality in patients with structural heart disease including DCM.

1. Introduction

Implantable cardiac defibrillators (ICDs) including cardiac resynchronization therapy devices capable of defibrillation (CRT-Ds), have become an established therapeutic option for reducing the risk of sudden cardiac death [1–5]. However, an ICD itself cannot prevent the occurrence of tachycardia attacks, and some patients may develop electrical storm (E-Storm) and receive shock deliveries or antitachycardia pacing (ATP) within a short period of time [6,7]. Patients who receive ICD shocks for termination of any arrhythmias have been shown to be associated with a substantially higher risk of death than patients who do not receive such shocks [8,9]. The incidence, predictive factors, and

Abbreviations: AF/AFL, atrial fibrillation and/or atrial flutter; ATP, antitachycardia pacing; CRT-D, cardiac resynchronization therapy device capable defibrillation; DCM, non-ischemic dilated cardiomyopathy; E-Storm, electrical storm; ICD, implantable cardiac defibrillator; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; VF, ventricular fibrillation; VT, ventricular tachycardia.

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clinical prognosis of patients with E-Storm were relatively well known in patients with ischemic heart disease (IHD) [10–13], but data are still lacking for other underlying heart diseases, especially in non-ischemic dilated cardiomyopathy (DCM).

The Nippon Storm Study was a prospective observational study designed to recruit clinical data from patients on ICD therapy [14,15] to investigate the incidence and the clinical characteristics of patients who develop E-Storm in Japan where DCM is relatively common compared to other Western countries.

2. Methods

2.1. Registration

The details of the overall study design of the Nippon Storm Study have been published [14,15]. Briefly, the Nippon Storm Study was organized by the Japanese Heart Rhythm Society and Japanese Society of Electrocardiology. Web site registration of patients was conducted in 48 Japanese ICD centers (Appendix A), and the Japanese Heart Rhythm Society collected data from physicians who input the patients' data. According to the guidelines for implantation of an ICD, indication and purpose of implantation was determined by attending cardiologists of each center.

2.2. ICD programing

The ICD was programmed at the physician's discretion. Some discrimination algorithms such as PR Logic and Wavelet (Medtronic, Minneapolis, MN), Rhythm ID (Boston Scientific, Marlborough, MA), and Morphology Discrimination plus AV Rate Branch (St. Jude Medical, St. Paul, MN) were used.

The ventricular fibrillation (VF) zone was >188 to 200 bpm with at least one train of ATP before the shock, and the ventricular tachycardia (VT) zone was >140 to 160 bpm with at least three trains of ATP before the shock, which were allowed to be modified according to patient's background.

Each E-Storm was managed by physicians according to their preference. If E-Storm was considered to be triggered by myocardial ischemia, heart failure, or electrolyte disorder, they were corrected immediately. If needed, an antiarrhythmic drug regimen comprising β-blockers, amiodarone, and lidocaine was administered sequentially or in combination. Some patients might undergo catheter ablation in the acute phase of E-Storm.

2.3. Follow-up

For the precise follow-up, we constructed a new tracking system called “Chaser” which was intended to minimize the loss of follow-up data. The data of interventions (both appropriate and inappropriate) from the ICD were sent at a maximum interval of 6 months, to the office of the Japanese Heart Rhythm Society through the Web site. The ICD interventions were classified into ATP, low-energy shocks, and high-energy shocks. E-Storm was defined as occurrence of at least three separate episodes of VT/VF within a 24-h period [6]. Every E-Storm was blindly adjudicated by two electro-physiologists (Drs. NA and KS) based on the intracardiac electrograms at the time of the event.

2.4. Data analysis

The patients' characteristics were analyzed from the baseline data which included age, sex, underlying heart disease, purpose of indication (primary or secondary), and complications related to implantation procedure.

As the main theme of this study, the incidence of E-Storm and its predictors were analyzed from the patients' baseline characteristics. Modalities of acute managements of E-Storm were analyzed. Finally, the prognosis was compared between the patients with and without E-Storm.

2.5. Statistics

Continuous baseline variables are presented as mean ± standard deviation, and categorical baseline variables are presented as n (%). When any two groups were compared, we applied the χ^2 test for categorical variables and Student's *t*-test for continuous variables. For time-to-event outcomes, survival curves were created using the Kaplan–Meier method, and log rank tests were used for statistical hypothesis tests. The effects of covariates were explored with proportional hazard models using the hazard ratio (HR) and 95% confidential interval (95% CI). To compare subsequent mortality between patients with and without E-Storm, survival curves adjusted for covariates were created using the inverse probability weighting method [16]. Because the times to E-Storm differed among patients, we also performed a landmark analysis at the 6-, 12-, and 18-month landmark points. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC). A p value of <0.05 was considered statistically significant.

This study was conducted in accordance with the Helsinki Declaration and proved by Institutional Review Board of each institution. All patients gave written informed consent to participate in this study.

3. Results

3.1. Patients' baseline characteristics

In total, 1570 patients from 48 ICD centers in Japan (Appendix A) were enrolled. Of these, we focused on 1274 patients with structural heart disease including 482 (38%) patients with IHD and 342 (27%) patients with DCM.

The baseline characteristics of the 1274 patients are outlined in Table 1. At the time of implantation, the patients were 65 ± 12 years old, and 967 (76%) of the patients were male. With respect to the indications for ICD implantation, 638 (50%) and 636 (50%) patients received an ICD for primary and secondary prevention of sudden cardiac death, respectively. An ICD was implanted in 775 (61%) patients, and a CRT-D was implanted in 499 (39%) patients. The mean left ventricular ejection fraction (LVEF) was 38%. Of 1274 patients, IHD ($n = 482$) and DCM ($n = 342$) were major causes of structural heart diseases.

3.2. Incidence of E-Storm

During a median follow-up of 28 (range, 23–33) months, E-Storm occurred in 84 (6.6%) patients (annual event rate 2.8%). Regarding the underlying heart diseases, E-Storm occurred in 24 (5.0%) patients with IHD, 21 (6.1%) patients with DCM, 13 (6.4%) patients with hypertrophic cardiomyopathy, 7 (24%) patients with arrhythmogenic right ventricular cardiomyopathy, and 19 (8.7%) patients with other structural heart disease including valvular heart disease, cardiac sarcoidosis, or congenital heart disease, etc. (Fig. 1A). With respect to the reason for the ICD indication, E-Storm occurred in 4.2% of the patients with primary prevention and in 9.0% of the patients with secondary prevention. In a survival analysis, the E-Storm-free survival curves did not differ between IHD and DCM patients (log-rank $p = 0.52$).

Table 1
Baseline characteristics of patients with ICD/CRT-D with structural heart disease ($n = 1274$).

Clinical characteristics	
Gender, man (%)	967 (76%)
Age years	65 ± 12
Underlying anatomic diagnosis	
IHD	482 (38%)
DCM	342 (27%)
HCM	204 (16%)
ARVC	29 (2%)
Other	218 (17%)
Primary prevention	638 (50%)
Secondary prevention	636 (50%)
ICD (%)	775 (61%)
CRT-D (%)	499 (39%)
NYHA I (%)	375 (29%)
NYHA II (%)	482 (38%)
NYHA III (%)	365 (29%)
NYHA IV (%)	52 (4%)
LVEF %	38 ± 17
Medication	
Beta-blocker (%)	887 (70%)
Amiodarone (%)	513 (40%)
ACEI or ARB	750 (59%)

ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; ARVC = arrhythmogenic right ventricular cardiomyopathy; CRT-D = cardiac resynchronization therapy device with defibrillator; DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; ICD = implantable cardiac defibrillator; ICSD = implantable cardiac shock device; IHD = ischemic heart disease; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association.