



Original article

Safety and efficacy of in-hospital cardiac rehabilitation following antiarrhythmic therapy for patients with electrical storm



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ARTICLE INFO

Article history:

Received 2 April 2018

Received in revised form 27 May 2018

Accepted 6 August 2018

Available online 17 October 2018

Keywords:

Cardiac rehabilitation

Electrical storm

Safety

ABSTRACT

Background: Exercise-based in-hospital rehabilitation for patients with electrical storm (ventricular tachycardia/ventricular fibrillation, VT/VF) following antiarrhythmic therapy may prevent the deleterious outcomes of prolonged immobility, but the safety and efficacy of this strategy are still uncertain. We retrospectively investigated the rate of electrical storm recurrence in patients receiving rehabilitation.

Methods: Sixty-seven patients receiving therapy for electrical storm were included in this study. After treatment, patients were divided into rehabilitation ($n = 39$) and non-rehabilitation ($n = 28$) groups.

Results: Incidences of electrical storm recurrence and VT/VF requiring anti-tachycardia pacing or electrical defibrillation did not differ significantly between the rehabilitation and non-rehabilitation groups (13% vs. 21% and 28% vs. 25%, respectively). However, early mobilization initiated ≤ 2 days after primary therapy was disadvantageous for electrical storm and VT/VF recurrence compared to later mobilization (21% vs. 6% and 34% vs. 19%, respectively). Although the activities of daily living (ADL) at admission were significantly lower in the rehabilitation group, the scores were restored to the level of the non-rehabilitation group at the time of discharge. Univariate analysis revealed that high B-type natriuretic peptide (hazard ratio [HR]: 3.2; 95% confidence interval [CI]: 1.1–11), decreased left ventricular ejection fraction, and elevated E/E' (HR: 3.4; 95% CI: 1.1–11) were associated with VT/VF recurrence.

Conclusions: The incidence of electrical storm relapse is substantial following antiarrhythmic therapy, but it is not increased by in-hospital rehabilitation. Although caution is urged for early mobilization, sustaining mobility to resume activity is recommended because ADL levels tend to deteriorate as a result of prolonged bed rest.

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Introduction

Electrical storm, also termed ventricular tachycardia (VT) or ventricular fibrillation (VF) storm, is a clinical condition characterized by an incessant outbreak of tachyarrhythmia within a short period of time [1]. Electrical storm is recognized as a medical emergency because the instability of ventricular arrhythmia can lead to sudden cardiac death [2]. Various therapeutic strategies,

including catheter ablation, can control ventricular arrhythmia and electrical storm, but all such treatments have limited therapeutic efficacy. Indeed, the early success rate of catheter ablation for electrical storm is 60–70% according to recent studies [3,4].

Since electrical storm recurrence must be expected based on current therapeutic efficacy, it is critical to investigate post-treatment care strategies with the aims of improving activities of daily living (ADL) level and facilitating safe discharge. To prevent problems associated with prolonged immobilization such as muscle atrophy, long-term and excessive bed rest should be avoided. In-hospital cardiac rehabilitation was first introduced for myocardial infarction patients in the 1950s to prevent the effects of

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prolonged bed rest [5]. Since then, the criteria for early cardiac rehabilitation have expanded so that patients with other forms of coronary heart disease, including heart failure, and following cardiovascular surgery are now considered eligible [6]. Hence, patients with arrhythmia can be included.

We routinely accept patients with a history of precarious events caused by ventricular arrhythmia, including those with electrical storm, for physical rehabilitation. Since there is insufficient evidence concerning the safety and efficacy of in-hospital cardiac rehabilitation, in this retrospective study we investigated its feasibility for patients with electrical storm, the most electrically unstable cardiac condition.

Methods

Study patients

Sixty-seven consecutive distinct patients exhibiting electrical storm and referred to the University of Tsukuba Hospital for antiarrhythmic treatment between June 2014 and May 2017 were included, and those who readmitted within this period of time due to VT/VF recurrence were excluded. Although there are multiple clinical definitions of electrical storm, generally accepted minimal criteria include (1) two or more VT/VF events occurring within 24 h in patients without an implantable cardioverter-defibrillator (ICD) or cardiac resynchronization therapy with a defibrillator (CRT-D) [7], and (2) implementation of three or more appropriate therapies for VT/VF, such as anti-tachycardia pacing (ATP) or electrical defibrillation, within 24 h in patients with an ICD or CRT-D [8–10]. Patients were grouped according to treatment as those receiving (1) medical treatment such as adjusting antiarrhythmic drug type/dose or ameliorating the condition of heart failure, (2) implantation of a device such as an ICD or CRT-D for secondary prevention, or (3) radiofrequency catheter ablation. In-hospital cardiac rehabilitation was provided for patients (rehabilitation group) who met all criteria as follows: (a) met the disease criteria for coverage by the National Health Insurance program of Japan; (myocardial infarction, angina pectoris, post open-heart-surgery, aortic disease, peripheral artery disease, or chronic heart failure [11]), (b) showed no relapse of the targeted tachyarrhythmia within 24 h of treatment, (c) were permitted to participate by their attending physician, and (d) provided consent. The remaining patients (non-rehabilitation group) received usual medical care without rehabilitation. Actually, the non-rehabilitation group indicated a heterogeneous entity consisting of patients who acquired a favorable clinical course without any disturbances in ADL level and who drastically exacerbated their conditions resulted in the disqualification of physical rehabilitation.

Clinical data, including laboratory, electrocardiography, echocardiography, and signal-averaged electrocardiography, were extracted from medical records. The Barthel index, a score of ADL [12], was measured by a trained medical professional at the time of admission and discharge. Ethical approval was obtained from the institutional review board of the University of Tsukuba Hospital, and all patients in the rehabilitation group gave their written informed consent before participation.

Rehabilitation protocol

The rehabilitation protocol was similar to that received by other cardiovascular disease patients at our institute. Patients initiated training by standing up from bed and attempting to walk with or without the aid of a walker. Walking distance was gradually prolonged according to impaired physical fitness to walk. Once patients were able to walk farther than 200 m, they participated in aerobic exercises using an ergometer. Physical exercise training

was provided once or twice daily, five times a week except for weekends. Every session was conducted under the supervision of medical staff such as a doctor, nurse, or physical therapist, with monitoring by telemetric electrocardiography. In the case of recurrent sustained VT/VF requiring ATP or electrical defibrillation, rehabilitation was immediately suspended until the attending physician allowed resumption based on a minimum of 24 h without further recurrence.

Statistics

Categorical variables are presented as frequencies and percentages. Continuous variables are presented as mean \pm standard deviation (SD) or median and interquartile range [IQR] depending on data distribution. Group differences in baseline categorical variables were compared using a chi-square test or Fisher's exact test as appropriate, and continuous variables were compared by an unpaired *t*-test, or Mann–Whitney *U* test, depending on distribution. The times to recurrence of electrical storm and VT/VF requiring ATP/electrical defibrillation from initiation of primary treatment to hospital day 30 were estimated by the Kaplan–Meier method, and the difference in survival rates was analyzed by the log-rank test. In this analysis, cases requiring repeat catheter ablation due to early recurrence were counted as additional distinct cases. Predictors of recurrent VT/VF necessitating ATP or electrical defibrillation were assessed by Cox regression models after verifying proportionality assumptions. Continuous variables were dichotomized based on institutional standard cut-off value. Only B-type natriuretic peptide (BNP) was divided based on a cut-off point using receiver operating characteristic curve because the vast majority of patients exceeded the institutional standard value. Candidate variables showing a significant association with recurrence ($p < 0.05$) in univariate analyses were included in multivariate regression models. For all analyses, $p < 0.05$ was considered statistically significant. Statistical assessment was performed using JMP[®] version 11 software (SAS Institute Inc., Cary, NC, USA) and R version 3.2.2 (R Foundation, Vienna, Austria).

Results

Patient characteristics

Of the 67 patients included, 58 (87%) were referred from other hospitals because of failure to manage their arrhythmia, and 26 (39%) of these referral patients required some form of nursing care due to a decline in exercise tolerance associated with the underlying diseases or prolonged bed-rest in the referring institute. Based on institutional criteria described above (Methods), in-hospital rehabilitation was initiated for patients who had finished treatment. In total, 39 (58%) patients received in-hospital cardiac rehabilitation, and the remaining 28 patients received only standard care. There were no patients with verified exercise-induced ventricular arrhythmia or catecholaminergic polymorphic ventricular tachycardia.

The rehabilitation group showed significantly lower baseline Barthel index values, while the distributions of other patient characteristics, including underlying heart diseases, comorbidities, and medical treatments on admission, were comparable between groups (Table 1). In addition, most clinical examination results did not differ significantly between groups. Also, the selected modalities of in-hospital treatment did not differ statistically, including catheter ablation for >70% of patients in both groups (Table 2). On the other hand, median length of hospital stay was significantly longer in the rehabilitation group (19 days [IQR: 11–28] vs. 12 days [IQR: 6–18]) because patients meeting rehabilitation group criteria took more time to recover their physical strength.

Table 1
Patient characteristics and clinical data at admission.

	Total group (n = 67)		Rehabilitation group (n = 39)		Non-rehabilitation group (n = 28)		p
	Mean Median n	(SD) [IQR] %	Mean Median n	(SD) [IQR] %	Mean Median n	(SD) [IQR] %	
Age, years	67	[58–73]	68	[63–73]	64	[51–73]	0.14
Male, n	57	85	36	92	21	75	0.08
BMI, kg/m ²	23	(3.9)	24	(4.1)	23	(3.7)	0.62
Barthel Index, points	68	[40–95]	60	[40–75]	90	[45–100]	0.02
NYHA class, n							0.17
III	23	34	17	44	6	21	
IV	7	10	3	7.7	4	14	
Type of arrhythmia, n							
VT	58	87	35	90	23	82	0.47
Previous number of catheter ablation for VT/VF					0.28		
0	43	64	23	59	20	71	
1	17	25	10	26	7	25	
≥2	7	10	6	15	1	4	
Underlying heart disease, n							
Ischemic	24	36	23	59	20	71	0.87
Old myocardial infarction	19	79	13	81	6	75	
Acute coronary syndrome	3	13	2	13	1	13	
Coronary spasm	2	8	1	6	1	13	
Non-ischemic	43	64	23	53	20	47	0.83
DCM	13	19	6	15	7	25	
HCM	9	13	6	15	3	11	
CS	5	7.5	2	5.1	3	11	
ARVC	1	1.5	1	2.6	0	0	
Others	11	16	6	15	5	18	
Idiopathic	4	6	2	5.1	2	7.1	1.0
Comorbidities, n							
DM	15	22	8	21	7	25	0.66
CKD	36	54	22	56	14	50	0.63
Paroxysmal AF	11	16	7	18	4	14	0.75
Persistent AF	7	10	2	5.1	5	18	0.12
Medication at admission, n							
β blocker	53	79	32	82	21	75	0.48
Amiodarone	30	45	18	46	12	43	0.79
Sotalol	11	16	8	21	3	11	0.34
Implantable electronic device, n							
ICD	27	36	18	46	9	32	0.25
CRT-D	15	20	7	18	8	29	0.3
Laboratory							
Albumin, g/dl	3.8	(0.6)	3.7	(0.6)	3.9	(0.7)	0.44
Creatinine, mg/dl	1.0	[0.8–1.3]	1.0	[0.8–1.3]	0.9	[0.8–1.5]	0.73
eGFR, ml/min/1.73 m ²	58	(25)	59	(25)	56	(26)	0.67
Sodium, mEq/l	139	[136–141]	139	[136–141]	139	[136–140]	0.46
Potassium, mEq/l	4.3	(0.5)	4.2	(0.3)	4.4	(0.7)	0.23
Hemoglobin, g/dl	13	(2.1)	13	(2.1)	13	(2.1)	0.87
Hb A1c, %	6.0	(0.8)	6.0	(0.7)	6.0	(0.8)	0.96
BNP, pg/ml	249	[83–496]	295	[104–581]	162	[69–456]	0.21
Electrocardiography							
QRS, ms	124	[104–162]	126	[111–168]	115	[100–152]	0.18
QT, ms	449	(55)	443	(51)	458	(60)	0.31
QTc, ms	479	(59)	470	(58)	490	(59)	0.18
Echocardiography							
LVEF, %	43	(16)	42	(16)	43	(16)	0.88
LAVI, ml/m ²	44	(20)	43	(21)	44	(18)	0.78
E/E'	10	[7.7–17]	11	[7.8–17]	8.7	[7.6–14]	0.42
TAPSE, mm	17	[13–20]	16	[12–18]	20	[17–22]	0.06
TRPG, mmHg	20	(8.9)	20	(8.5)	21	(9.7)	0.73
Aneurysm, n	21	33	16	43	5	19	0.04
Signal-averaged electrocardiography							
3/3 points, n	37	66	24	69	13	62	0.77

Data presented as mean (SD), or median [interquartile range], or n %.

p-Value represents a test of equality between the rehabilitation group and non-rehabilitation group.

3/3 points in signal-averaged electrocardiography met all of the requirements as follows: total filtered QRS duration greater than 105 msec, a root mean square voltage in the terminal 40 ms of less than 15 μV, and the duration of signals less than 40 μV of greater than 39 ms.

BMI, body mass index; NYHA, New York Heart Association; VT, ventricular tachycardia; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; CS, cardiac sarcoidosis; ARVC, arrhythmogenic right ventricular cardiomyopathy; DM, diabetes mellitus; CKD, chronic kidney disease; AF, atrial fibrillation; ICD, implantable cardioverter-defibrillator; CRT-D, cardiac resynchronization therapy with defibrillator; eGFR, estimated glomerular filtration rate; BNP, B-type natriuretic peptide; QTc, corrected QT interval; LVEF, left ventricular ejection fraction; LAVI, left atrial volume index; E/E', mitral early diastolic velocity/average early diastolic E' velocity ratio; TAPSE, tricuspid annular plane systolic excursion; TRPG, tricuspid regurgitation peak gradient.

Table 2
Selected treatment(s).

	Total group (n = 67)		Rehabilitation group (n = 39)		Non-rehabilitation group (n = 28)		p
	n	%	n	%	n	%	
Medication	3	4	3	8	0	0	0.39
Device implantation	11	16	6	15	5	18	
RFCA	44	66	25	64	19	68	
RFCA and device implantation	9	13	5	13	4	14	

Data presented as n %.
p-Value represents a test of equality between rehabilitation group and non-rehabilitation group.
RFCA, radiofrequency catheter ablation.

Safety

During hospitalization, electrical storm recurred in 13% (5/39) of the rehabilitation group patients compared with 21% (6/28) of the non-rehabilitation group patients. Recurrence of VT/VF requiring ATP or electrical defibrillation occurred in 28% (11/39) of the rehabilitation group patients, and 25% (7/28) of non-rehabilitation group patients. Only one case of VT recurrence occurred during an actual rehabilitation session. Kaplan–Meier analysis revealed no differences in recurrence rates between groups (Fig. 1). Of the recurrent cases, eight patients received repeat catheter ablation. There were three fatalities due to uncontrollable arrhythmia and cardiogenic shock in the non-rehabilitation group, but none in the rehabilitation group.

The median interval between primary treatment and initiation of cardiac rehabilitation was 2 days (IQR: 1–3 days). Patients receiving in-hospital rehabilitation were divided based on this interval, and we classified these patients receiving rehabilitation within 2 days as the Early Rehabilitation Group (27/39, 69%) and the others as the Late Rehabilitation Group (12/39, 31%). Main reasons for delays in the latter group were subsequent medical procedures (5/12, 42%), unstable patient conditions (4/12, 33%), and weekend hospital management (3/12, 25%). Kaplan–Meier

analysis revealed that prognosis was negatively affected by early rehabilitation, as this group exhibited higher recurrence of electrical storm and VT/VF requiring ATP or electrical defibrillation (21% vs. 6% and 34% vs. 19%, respectively [Fig. 2]), even though patient background parameters were comparable except for length of hospital stay, serum albumin concentration, and renal function (Supplementary Table).

Efficacy

The median total time of physical rehabilitation was 9.9 h (IQR: 4–12.8 h) and the median number of days was 10 (IQR: 7–19). Thirty-four rehabilitation patients (89%) were able to advance to aerobic training using an ergometer after walking more than 200 m with or without assistance.

The Barthel index was lower in the rehabilitation group at the time of admission, but it did not differ from that of the non-rehabilitation group at the time of discharge (group difference in Δ Barthel index: 30 ± 25 vs. 11 ± 23 , $p < 0.01$ [Fig. 3]). Also, the improvement of the Barthel index from admission to discharge did not differ between the Early and Late Rehabilitation Group (29 ± 24 vs. 30 ± 26 , $p = 0.91$). Moreover, ambulatory performance and clinical outcome were also comparable between the rehabili-

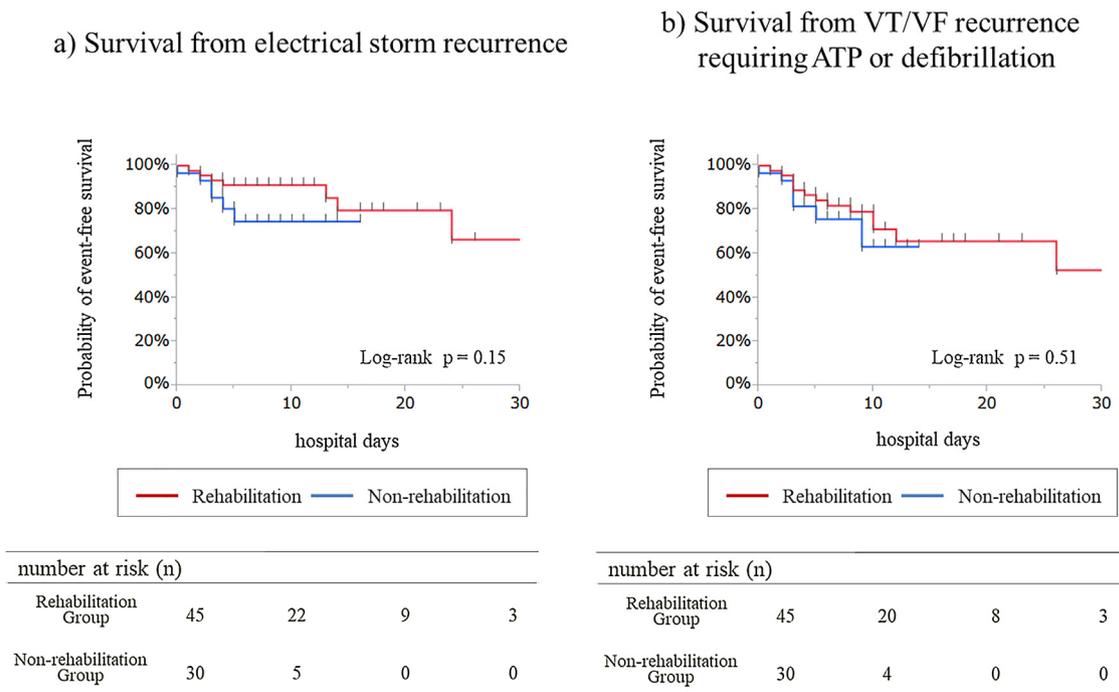


Fig. 1. Kaplan–Meier curves of event-free survival for rehabilitation and non-rehabilitation groups. (a) Electrical storm recurrence in rehabilitation and non-rehabilitation groups. (b) Incidence of ventricular tachyarrhythmia requiring anti-tachycardia pacing (ATP) or electrical defibrillation in each group.

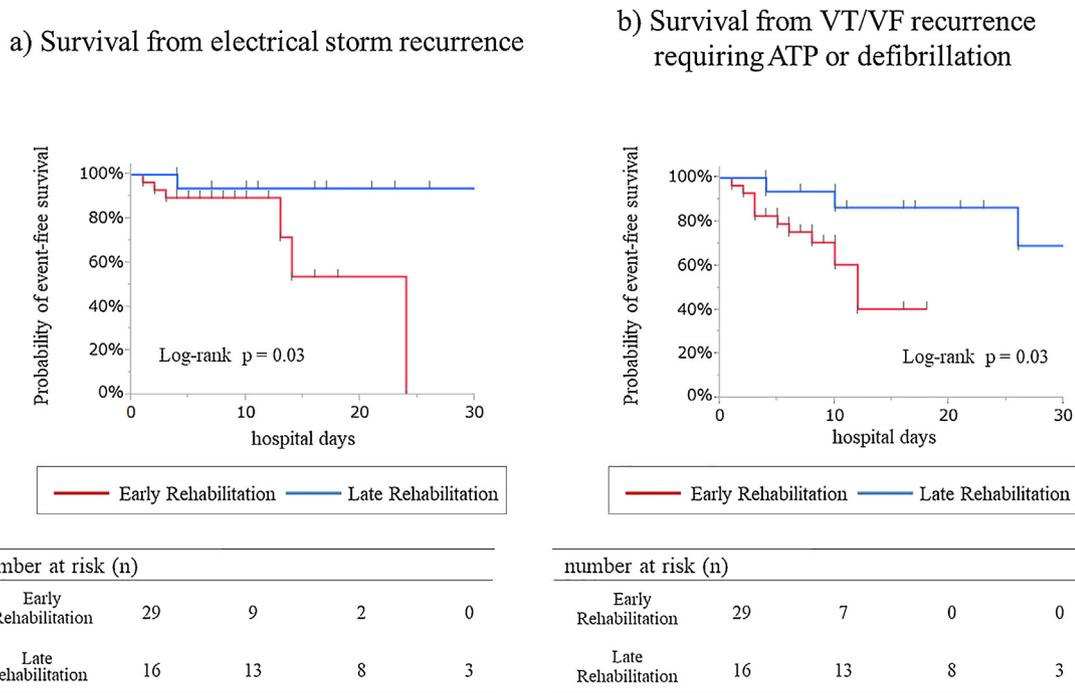


Fig. 2. Kaplan–Meier curves of event-free survival for early and late rehabilitation groups. (a) Electrical storm recurrence in early rehabilitation and late rehabilitation groups. (b) Recurrence of ventricular tachyarrhythmia requiring anti-tachycardia pacing (ATP) or electrical defibrillation.

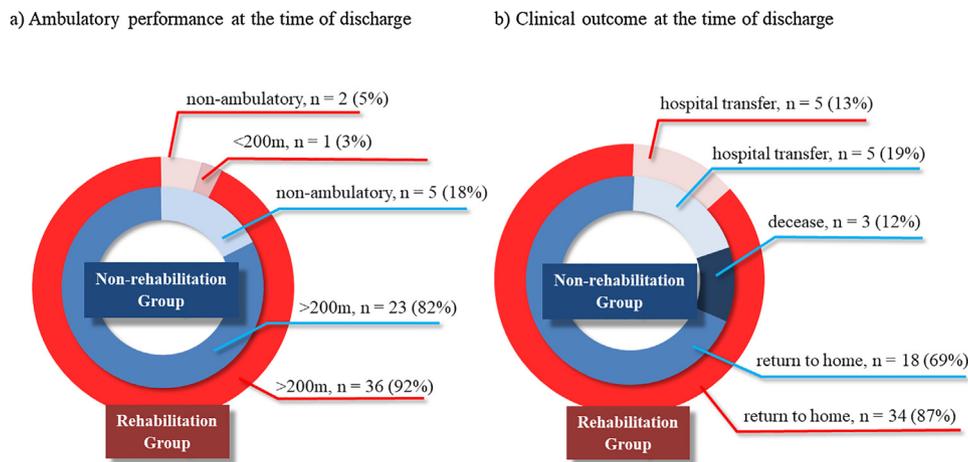


Fig. 3. Changes in Barthel activities of daily living (ADL) index values from admission to discharge in each group. Plotted data are shown as the distribution and mean ± SD.

tation and non-rehabilitation groups at the time of discharge (Fig. 4).

Risk assessment

Univariate analysis of candidate factors potentially associated with recurrence of VT/VF requiring ATP or electrical defibrillation identified increased BNP (hazard ratio [HR]: 3.2; 95% confidence interval [CI]: 1.1–11), low left ventricular ejection fraction (LVEF) (HR: 4.5; 95% CI: 1.3–29) and elevated ratio of mitral early diastolic velocity to average early diastolic E' velocity (E/E') (HR: 3.4; 95% CI: 1.1–11) as potential prognosticators in the entire group; however, there was no significant influence of rehabilitation (Fig. 5). On the other hand, multivariate analysis failed to identify an independent predictor of VT/VF recurrence among the variables with significance in the univariate analysis.

Discussion

In the present study, we demonstrate the feasibility of in-hospital cardiac rehabilitation for post-treatment patients exhibiting electrical storm, known as the most hazardous arrhythmic state. While recurrence risk was clinically significant in both rehabilitation and non-rehabilitation groups, it was not increased by physical rehabilitation. However, early mobilization was associated with less favorable prognosis. Further, increased BNP, low LVEF, and elevated E/E' were potential predictors of ventricular tachyarrhythmia recurrence, which will contribute to risk stratification in this patient group.

Cardiac rehabilitation is now practiced throughout the world, driven by reports of safety and effectiveness [13]. However, safety has been demonstrated mainly in an outpatient setting. Indeed, such investigations have reported an outpatient cardiovascular

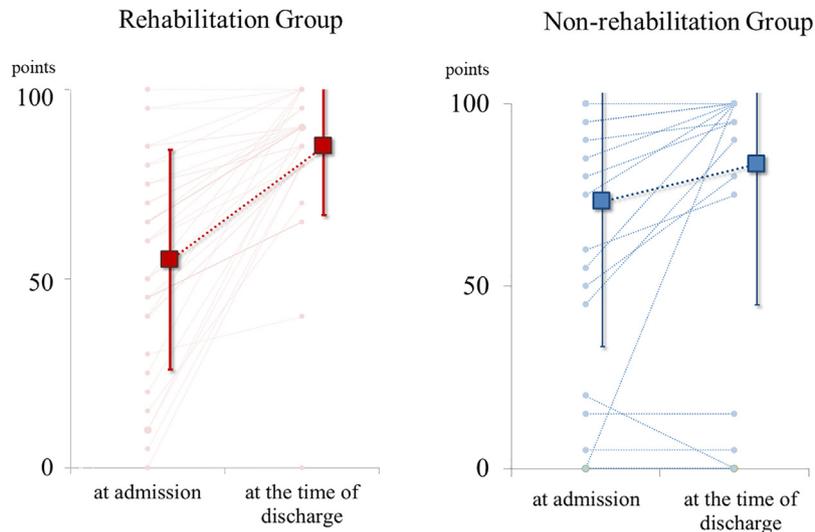


Fig. 4. Comparisons of (a) ambulatory performance at the time of hospital discharge, and (b) clinical outcome in each group.

	Number	HR	95% C.I	0.01	0.1	1	10	100	p
Age									
>60 years	50/67	1.7	(0.5–11)						0.44
BMI									
<18.5 kg/m	5/66	0.8	(0.04–3.9)						0.8
>25 kg/m	18/66	0.7	(0.2–2.2)						0.58
NYHA class									
III-IV	30/67	1.6	(0.6–4.3)						0.38
Underlying heart disease									
IHD	24/67	1.2	(0.5–3.6)						0.91
Comorbidities									
DM	15/67	1.2	(0.4–3.2)						0.69
CKD	36/67	0.8	(0.3–2.3)						0.67
AF	18/67	2.2	(0.8–5.8)						0.14
Medication									
Amiodarone	30/67	1.1	(0.4–3)						0.82
Sotalol	11/67	1.5	(0.4–4.4)						0.46
Laboratory									
Albumin <3.8 g/dl	28/67	1.1	(0.4–3)						0.83
Sodium <135 mEq/l	12/67	2.2	(0.7–5.8)						0.15
Potassium <4 mEq/l	13/67	0.9	(0.2–2.8)						0.87
Hemoglobin									
<14 g/dl (male), <12 g/dl (female)	38/67	2.1	(0.8–7.6)						0.16
BNP >255 pg/ml	33/67	3.2	(1.1–11)						0.03
Electrocardiogram									
QRS >150 ms	20/67	1.2	(0.4–3.2)						0.75
QT >470 ms	21/67	2.3	(0.8–6.3)						0.1
QTc >440 ms	49/67	0.9	(0.3–3.2)						0.89
Echocardiogram									
LVEF <45%	35/67	4.5	(1.3–29)						0.02
LAVI >40 ml/m	32/63	3.1	(0.9–14)						0.07
E/E' >15	17/56	3.4	(1.1–11)						0.03
TAPSE <16 mm	7/26	2.9	(0.6–15)						0.17
aneurysm	21/64	1.2	(0.4–3.3)						0.89
Signal-averaged electrocardiogram									
3/3 points	37/56	0.8	(0.3–2.8)						0.77

Fig. 5. Univariate Cox proportional analysis of candidate factors associated with recurrent ventricular tachyarrhythmia requiring anti-tachycardia pacing or electrical defibrillation. Abbreviations: BMI, body mass index; NYHA, New York Heart Association; IHD, ischemic heart disease; DM, diabetes mellitus; CKD, chronic kidney disease; AF, atrial fibrillation; LAVI, left atrial volume index; TAPSE, tricuspid annular plane systolic excursion; other abbreviations as in the text.

event rate, including cardiac arrest and myocardial infarction, of only one per 26,715–81,101 patient-hours during exercise [14–17]. In contrast, existing evidence suggests that in-hospital rehabilitation is less safe. According to a report from a Korean institution in which >90% of enrolled patients had coronary artery disease, the event rate in an inpatient setting was one per 820 patient-hours under supervised exercise [18]. In the current study, 13 VT/VF recurrent episodes occurred, but only one occurred during exercise training (corresponding to one event per 408 patient-hours). Therefore, acute phase recurrence following antiarrhythmic therapy is relatively high with or without rehabilitation.

This result does not imply that in-hospital rehabilitation is safer for patients with electrical storm, even following sufficient therapies, compared with other cardiovascular diseases. Current guidelines suggest earliest possible in-hospital rehabilitation following adequate coronary revascularization and heart surgery [19], but controversies remain regarding the safety of mobilization for ventricular tachyarrhythmia patients, especially those with electrical storm due to the concern that physical exercise will increase arrhythmic recurrence. Since patients are often forced to restrict inpatient activity based on physician's orders, they may remain sedentary after leaving hospital out of fear of recurrence. Therefore, in-hospital rehabilitation for such patients may still be

of benefit since it prevents further atrophy and other sequelae of prolonged immobility, and this prevention may remove psychological burdens to aid in resuming activity by mitigating physical impediments.

The three major findings of the present study are summarized below. First, this unique investigation supports the feasibility of physical rehabilitation for patients with ventricular tachyarrhythmia. Indeed, the rehabilitation group showing non-inferiority of VT/VF recurrences frequency compared with the non-rehabilitation group offers hope for the spread of this methodology. In addition, early mobilization, which is concordant with current trends in rehabilitation medicine, led to increased recurrent arrhythmic events. Myocardial irritability due to inflammation by catheter ablation and mechanical stimuli by anchored electrode may be present after antiarrhythmic therapy. In addition, physical exercise during this period probably inflames heart arrhythmogenic excitability via the intrinsic catecholaminergic reaction. Therefore, within a certain period of susceptible time, caution is recommended when introducing early mobilization. Further, the minimum number of days before the safe initiation of physical therapy remains unclear in this study.

Second, in-hospital rehabilitation plays a crucial role in restoring deteriorated ADL level to self-sustaining levels by the time of discharge, and this factor should weigh against any increase in arrhythmic recurrence risk. This improvement of clinical outcome provides additional validation for the use of in-hospital rehabilitation as an essential component of post-treatment care for VT/VF patients. Although we did not assess differences in the quality of life (QOL) and psychological status in this study, previous studies have reported that mental disorders such as depression negatively impact heart rhythm [20,21]. In practice, we have noted both physical and psychological improvements in patients receiving in-hospital rehabilitation, possibly resulting from an enhanced sense of self-efficacy. Maintaining physical fitness and independent living may be critical for improving the long-term prognosis of patients with ventricular tachyarrhythmia.

Third, we also identified potential risk factors for recurrence among patients with electrical storm. High BNP, low LVEF, and elevated E/ E' were associated with recurrence of VT/VF requiring ATP or electrical defibrillation in univariate analysis. Multivariate analysis failed to reveal independence of any of these explanatory variables, possibly because these variables may offset as covariants. Our results are in accord with previous findings that advanced left ventricular dysfunction enhances the excitability of cardiomyocytes [22,23]. Moreover, both high BNP and elevated E/ E' are associated with hemodynamic congestion in patients with heart failure. Sub-analysis of the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II) revealed that exacerbation of heart failure was closely linked to ventricular arrhythmia in patients with ICD [24] because cardiac excitability increases through elevated cardiac sympathetic activity or elevation of ventricular filling pressure. Accordingly, deteriorated left ventricular function or impaired hemodynamics could be causative factors for recurrence of ventricular arrhythmia and should be considered when considering physical rehabilitation for patients with electrical storm.

Study limitations

The present study has several limitations. This was a single-center, retrospective, observational study of a relatively small patient sample. Even though most patient characteristics were comparable, other differences between groups may have obscured certain benefits or disadvantages of in-hospital rehabilitation. While this study was retrospective and inconclusive regarding the

benefits of early in-hospital cardiac rehabilitation for patients with severe ventricular arrhythmia, the demonstration of non-inferiority warrants a larger-scale multicenter study to address these issues. In addition, the safety of more vigorous exercise training could not be ensured because not all patients were evaluated with an exercise stress test. The primary aim of in-hospital rehabilitation, however, was to reestablish physical activity safely for hospital discharge, not to improve physical fitness to the same extent as outpatient rehabilitation programs for secondary prevention.

Conclusion

The risk of VT/VF recurrence is clinically significant in electrical storm patients with or without in-hospital cardiac rehabilitation. Although early mobilization increased VT/VF recurrence risk in this study, and in-hospital rehabilitation appears to benefit patients as well by improving physical strength and clinical outcome. The results of the present study provide a foundation for the development of improved in-hospital cardiac rehabilitation methods.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jcc.2018.08.004.

References

- [1] Exner DV, Pinski SL, Wyse DG, Renfro EG, Follmann D, Gold M, et al. Antiarrhythmics versus implantable defibrillators. Electrical storm presages non-sudden death: the antiarrhythmics versus implantable defibrillators (AVID) trial. *Circulation* 2001;103:2066–71.
- [2] Carbucicchio C, Santamaria M, Trevisi N, Maccabelli G, Giraldo F, Fassini G, et al. Catheter ablation for the treatment of electrical storm in patients with implantable cardioverter-defibrillators: short- and long-term outcomes in a prospective single-centre study. *Circulation* 2008;117:462–9.
- [3] Aldhoon B, Wichterle D, Peichl P, Čihák R, Kautzner J. Outcomes of ventricular tachycardia ablation in patients with structural heart disease: the impact of electrical storm. *PLoS One* 2017;12:e0171830.
- [4] Nayyar S, Ganesan AN, Brooks AG, Sullivan T, Roberts-Thomson KC, Sanders P. Venturing into ventricular arrhythmia storm: a systematic review and meta-analysis. *Eur Heart J* 2013;34:560–71.
- [5] Bethell HJ. Cardiac rehabilitation: from Hellerstein to the millennium. *Int J Clin Pract* 2000;54:92–7.
- [6] Bethell H, Lewin R, Dalal H. Cardiac rehabilitation in the United Kingdom. *Heart* 2009;95:271–5.
- [7] Kowey PR, Levine JH, Herre JM, Pacifico A, Lindsay BD, Plumb VJ, et al. Randomized, double-blind comparison of intravenous amiodarone and bretylium in the treatment of patients with recurrent, hemodynamically destabilizing ventricular tachycardia or fibrillation. *Circulation* 1995;92:3255–63.
- [8] Gao D, Sapp JL. Electrical storm: definitions, clinical importance, and treatment. *Curr Opin Cardiol* 2013;28:72–9.
- [9] Israel CW, Barold SS. Electrical storm in patients with an implanted defibrillator: a matter of definition. *Ann Noninvasive Electrocardiol* 2007;12:375–82.
- [10] Credner SC, Klingeneben T, Mauss O, Sticherling C, Hohnloser SH. Electrical storm in patients with transvenous implantable cardioverter-defibrillators: incidence, management and prognostic implications. *J Am Coll Cardiol* 1998;32:1909–15.
- [11] JCS Joint Working Group. Guidelines for rehabilitation in patients with cardiovascular disease (JCS 2012). *Circ J* 2014;78:2022–93.
- [12] Sainsbury A, Seebass G, Bansal A, Young JB. Reliability of the Barthel Index when used with older people. *Age Ageing* 2005;34:228–32.
- [13] Pashkow FJ. Issues in contemporary cardiac rehabilitation: a historical perspective. *J Am Coll Cardiol* 1993;21:822–34.

- [14] Pavy B, Iliou MC, Meurin P, Tabet JY, Corone S. Safety of exercise training for cardiac patients: results of the French registry of complications during cardiac rehabilitation. *Arch Intern Med* 2006;166:2329–34.
- [15] Haskell WL. Cardiovascular complications during exercise training of cardiac patients. *Circulation* 1978;57:920–4.
- [16] Van Camp SP, Peterson RA. Cardiovascular complications of outpatient cardiac rehabilitation programs. *JAMA* 1986;256:1160–3.
- [17] Saito M, Ueshima K, Saito M, Iwasaka T, Daida H, Kohzuki M, et al. Safety of exercise-based cardiac rehabilitation and exercise testing for cardiac patients in Japan: a nationwide survey. *Circ J* 2014;78:1646–53.
- [18] Kim C, Moon CJ, Lim MH. Safety of monitoring exercise for early hospital-based cardiac rehabilitation. *Ann Rehabil Med* 2012;36:262–7.
- [19] Lichtman SW, American Association of Cardiovascular and Pulmonary Rehabilitation. Cardiac rehabilitation in the inpatient and transitional settings. In: *Guidelines for cardiac rehabilitation and secondary prevention programs*. fifth ed. Champaign/IL: Human Kinetics Publishers; 2013. p. 41–56.
- [20] Whang W, Albert CM, Sears Jr SF, Lampert R, Conti JB, Wang PJ, et al. Depression as a predictor for appropriate shocks among patients with implantable cardioverter-defibrillators: results from the Triggers of Ventricular Arrhythmias (TOVA) study. *J Am Coll Cardiol* 2005;45:1090–5.
- [21] Shi S, Liu T, Liang J, Hu D, Yang B. Depression and risk of sudden cardiac death and arrhythmias: a meta-analysis. *Psychosom Med* 2017;79:153–61.
- [22] Streitner F, Kuschyk J, Veltmann C, Mahl E, Dietrich C, Schimpf R, et al. Predictors of electrical storm recurrences in patients with implantable cardioverter-defibrillators. *Europace* 2011;13:668–74.
- [23] Santangeli P, Frankel DS, Tung R, Vaseghi M, Sauer WH, Tzou WS, et al. Early mortality after catheter ablation of ventricular tachycardia in patients with structural heart disease. *J Am Coll Cardiol* 2017;69:2105–15.
- [24] Singh JP, Hall WJ, McNitt S, Wang H, Daubert JP, Zareba W, et al. Factors influencing appropriate firing of the implanted defibrillator for ventricular tachycardia/fibrillation: findings from the Multicenter Automatic Defibrillator Implantation Trial II (MADIT-II). *J Am Coll Cardiol* 2005;46:1712–20.