Internal Medicine
The Japanese Society of Internal Medicine
doi: 10.2169/internalmedicine.1905-18
Intern Med 58: 2333-2340, 2019
http://internmed.jp

【 ORIGINAL ARTICLE 】

# A Low Critical Event Rate Despite a High Abnormal Event Rate in Patients with Cardiac Implantable Electric Devices Followed Up by Remote Monitoring

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**Abstract:**

**Objective** Remote monitoring (RM) of cardiac implantable electric devices (CIEDs) has been advocated as a healthcare standard. However, expert consensus statements suggest that all patients require annual face-to-face follow-up consultations at outpatient clinics even if RM reveals no episodes. The objective of this study was to determine the critical event rate after CIED implantation through RM.

**Methods** This multicenter, retrospective, cohort study evaluated patients with pacemakers (PMs), implantable cardioverter defibrillators (ICDs), or cardiac resynchronization therapy defibrillator (CRT-Ds) and analyzed whether or not the data drawn from RM included abnormal or critical events.

**Patients** A total of 1,849 CIED patients in 12 hospitals who were followed up by the RM center in Okayama University Hospital were included in this study.

**Results** During the mean follow-up period of 774.9 days, 16,560 transmissions were analyzed, of which 11,040 (66.7%) were abnormal events and only 676 (4.1%) were critical events. The critical event rate in the PM group was significantly lower than that in the ICD or CRT-D groups (0.9% vs. 5.0% or 5.9%, $p<0.001$). A multivariate analysis revealed that ICD, CRT-D, and a low ejection fraction were independently associated with critical events. In patients with ICD, the independent risk factors for a critical event were old age, low ejection fraction, Brugada syndrome, dilated phase hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy.

**Conclusion** Although abnormal events were observed in two-thirds of the transmitted RM data, the critical event rate was <1% in patients with a PM, which was lower in comparison to the rates in patients with ICDs or CRT-Ds. A low ejection fraction was an independent predictor of critical events.

**Key words:** remote monitoring, pacemaker, implantable cardioverter defibrillator, cardiac resynchronization therapy with defibrillator

**(Intern Med 58: 2333-2340, 2019)**
**(DOI: 10.2169/internalmedicine.1905-18)**

## Introduction

Remote monitoring (RM) of cardiac implantable electric devices (CIEDs) has been rapidly advocated as a new healthcare standard for patients with CIEDs. Several large, prospective, randomized trials of RM of patients with CIEDs have demonstrated its safety, feasibility, efficacy, as well as an association with improved survival (1-4). Expert consensus statements (5, 6) suggest that all patients with CIEDs should be offered RM as part of the standard follow-up management strategy. However, expert consensus state-

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Received: August 1, 2018; Accepted: February 21, 2019; Advance Publication by J-STAGE: May 22, 2019
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ments (5, 6) also suggest that all patients require annual face-to-face follow-up examinations at outpatient clinics even if RM reveals no episodes. Because the number of CIEDs has been constantly increasing (7, 8), the workload of outpatient clinics has not been markedly reduced. As previously reported, various abnormal events are detected by CIEDs follow-up, including atrial tachyarrhythmia (ATA), ventricular tachyarrhythmia (VTA), lead failure, and abnormal battery events (1-4). However, the number of CIED patients who did not require intervention and did not need to visit an outpatient clinic was very large. If the selection of patients for CIED follow-up could be limited to those who require intervention, such as those who require additional medication or a change of medication, a change in programming, implantation of new leads, or the exchange of generator, the workload involved would dramatically decrease. To do this, determining the critical event rate in various categories and the categories that should be the focus of attention is important. The aim of the study was to evaluate whether the critical event rate differed according to various factors, including age, sex, CIED type and manufacturer, underlying heart disease, and ejection fraction.

## Materials and Methods

### Patient population

CIED patients in 12 hospitals (The Sakakibara Heart Institute of Okayama, Okayama Medical Center, Fukuyama Cardiovascular Hospital, Fukuyama City Hospital, Iwakuni Medical Center, Tsuyama Chuo Hospital, Kagawa Prefectural Central Hospital, Kochi Medical Center, Takamatsu Red Cross Hospital, Okayama Red Cross Hospital, Onomichi City Hospital, and Okayama University Hospital) who were followed up by the RM center in Okayama University Hospital were included in this study. The CIEDs included pacemakers (PM), implantable cardioverter defibrillators (ICDs), and cardiac resynchronization therapy defibrillators (CRT-D). The RM systems were based on periodic remote follow-ups with automatic alerts [Medtronic CareLink (MCL), Minneapolis, USA; Abbott Medical Merlin (AMM) (9), Sylmar, USA; Boston Scientific Latitude (BSL), St. Paul, USA; BIOTRONIK Home Monitoring (BHM), Berlin, Germany]. Patients who could not visit any hospital were excluded. All patients gave their written informed consent for RM, and the study protocol was approved by the Institutional Review Board and/or the Medical Ethics Committee of each hospital.

### Study design and event definitions

This was a retrospective, multicenter, cohort study. RM data were manually or automatically transmitted based on each RM system. The durations of the periodic transmission schedules were different (every 1-4 months) in each hospital. All data transmitted by RM were analyzed and summarized by medical engineers and doctors in the RM center, focusing mainly on arrhythmic and device-related events. Abnormal events were defined as ATA events, VTA events, abnormal battery voltage events (reaching less than 1 year of expected battery life or <10%), electrical abnormal events related to the leads, and others, based on the diagnosis of each device. Although the CIED diagnosis of tachyarrhythmia was sometimes wrong, the CIED diagnosis was unchanged. The reasons were that it was difficult to precisely diagnose what the tachycardia was, even though it was carefully analyzed, and the focus of this study was on critical events, not abnormal events. Only the numbers of ATA, VTA, and abnormal battery events are shown because there were many manufacturer-specific abnormal events, including a short-VV-interval counter, noise reversion, OptiVol, CorVue, and the count of premature ventricular contractions.

Abnormal events were also classified as critical or non-critical events. Critical events were defined as appropriate/inappropriate ICD therapy (including ICD shock or anti-tachycardia pacing), battery depletion reaching the elective replacement indicator, lead impedance abnormality (increase in pace/sense conductor impedance >1,500 Ω or decrease in pace/sense conductor impedance <200 Ω, change in high-voltage lead impedance >125 or <20 Ω), non-physiological noise, atrial or ventricular sensing failure, atrial or ventricular pacing failure, reduction of P- or R-wave sensing amplitude by 50% of the safety margin, acutely increased atrial or ventricular pacing threshold (capture threshold >5 V or an increase in capture threshold >2 V from baseline <1 V), sustained ventricular tachycardia out of the therapy zone, and others. Previous randomized studies reported that CIEDs could detect subclinical atrial fibrillation (AF) (10) much earlier (1, 3, 6, 11). However, because the strategy for antithrombotic therapy of subclinical AF has not been established, these events were not included as critical events in the present study. Similarly, alerts related to heart failure were excluded. Previous trials (12, 13) demonstrated the efficacy of RM as a diagnostic tool for heart failure. However, controversial results (14, 15) have also been reported, and the clinical diagnostic parameters have not been well established. The expert consensus statement (6) indicates that the use of RM as a diagnostic tool for heart failure is a class IIb recommendation.

### Statistical analysis

Continuous data were summarized as the mean and standard deviation, were compared among groups using the Kruskal-Wallis test. Categorical data were summarized as the frequencies and percentages, and were compared using Pearson's chi-squared test. To account for correlations between repeated transmission measurements within patients, the generalized estimating equation (GEE) was used with a compound symmetry working correlation structure. Transmission data were compared among groups, and p values were calculated using GEE models. Multivariate analyses were performed to evaluate the correlations between covariates and critical events, and odds ratios with their 95% con-

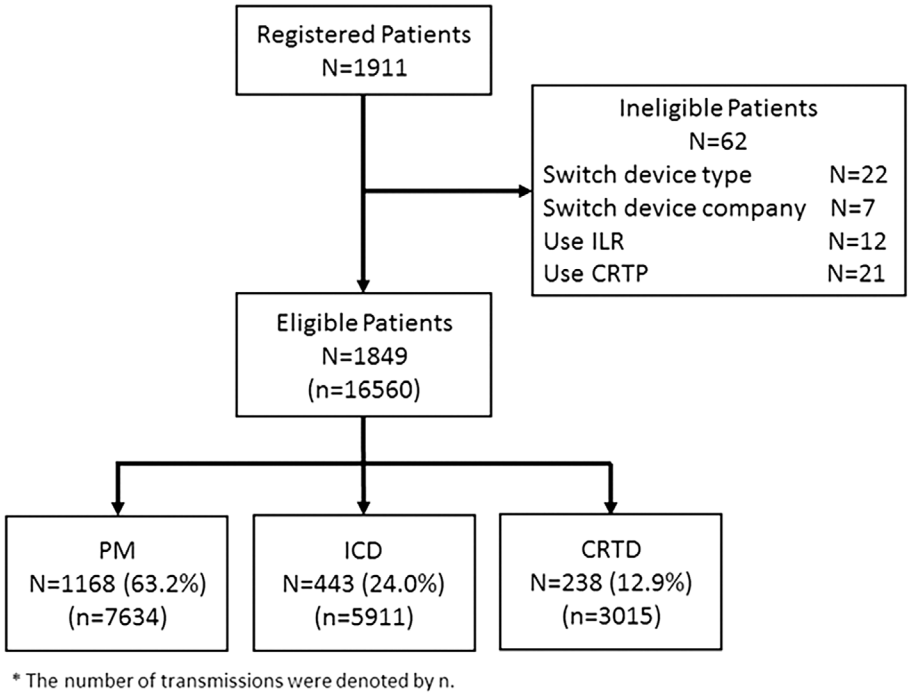


**Figure. Patient population. Twelve patients with implantable loop recorders, 22 patients whose CIED generator type was exchanged, 7 patients whose generator manufacturer was changed, and 21 patients with CRT-P were excluded. The remaining 1,849 patients, including 1,168 PM, 443 ICD, and 238 CRT-D patients, were enrolled in this study. CIED: cardiac implantable electronic devices, CRT-P: cardiac resynchronization therapy pacemaker, PM: pacemaker, ICD: implantable cardioverter defibrillator, CRT-D: cardiac resynchronization therapy defibrillator**

fidence intervals and p values were calculated using a multivariate GEE model. All tests were two-sided, and p values of <0.05 were considered to indicate statistical significance. All statistical analyses were performed by SAS version 9.4 (SAS Institute, Cary, USA).

## Results

### Patient population

A total of 1,911 patients with CIEDs were registered in our database between August 2009 and March 2016. Forty-one patients were excluded due to loop recorder implantation (n=12), change in CIED generator (n=22), and change in generator manufacturer (n=7). Twenty-one patients with cardiac resynchronization therapy pacemakers (CRT-Ps) were further excluded because the number of patients with CRT-Ps was too small to be analyzed accurately. Thus, 1,849 patients [PM, n=1,168 (63.2%); ICD, n=443 (24.0%); and CRT-D, n=238; (12.9%)] patients, were analyzed (Figure).

### Patient characteristics and remote transmissions

During a mean follow-up period of 774.9±652.9 days, 16,560 transmissions in 1,849 patients were analyzed in the RM center. The mean age of the patients was 71.6±14.6 years; the mean ejection fraction was 57.7±16.2%, and 1,024 (55.4%) patients were male. The baseline patient characteristics are shown in Table 1. Younger patients were more common in the ICD group than in the other groups, and fewer male patients were included in the PM group than in the other groups. The number of transmissions per patient was greater in ICD or CRT-D patients than in PM patients. The follow-up period in the PM group was shorter than that in the other groups. The proportions of CIED types differed among the manufacturers (Table 1).

### Abnormal events

At least one abnormal event was observed in approximately two-thirds of the data transmissions (11,040/16,565, 66.7%). The abnormal event rate in the CRT-D group was significantly greater than that in the other groups. Among the abnormal events, ATA events were most frequently observed (n=5,981, 36.1%), followed by VTA events (n=3,753, 22.7%) and abnormal battery voltage events (n=334, 2.0%). The ATA event rate was significantly lower in ICD patients, the VTA event rate was significantly lower in PM patients, and the abnormal battery voltage event rate was significantly lower in PM patients (Table 2).

### Critical events

The critical event rate was only 4.1% (676/16,560). The critical event rate was significantly lower in PM patients (0.9%) than in ICD (6.6%) or CRT-D (7.3%) patients. Among the three types of CIEDs, a major difference was observed in the critical event rate in ICD therapy (ICD,

**Table 1. Patient Characteristics.**

| Variable | Overall (n=1,849) | PM (n=1,168) | ICD (n=443) | CRT-D (n=238) | p value |
|---|---|---|---|---|---|
| Gender | | | | | |
| Male | 1,024 (55.4) | 530 (45.4) | 333 (75.2) | 161 (67.6) | <0.0001[a] |
| Age (years) | 71.6±14.6 | 77.6±10.7 | 58.3±15.7 | 67.4±10.8 | <0.0001[b] |
| Indication for pacemaker | | | | | |
| AVB | 603/1,205 (50.0) | 570/1,145 (49.8) | 9 (42.9) | 24 (61.5) | - |
| SSS | 504/1,205 (41.8) | 488/1,145 (42.6) | 9 (42.9) | 7 (17.9) | |
| AF brady | 76/1,205 (6.3) | 75/1,145 (6.6) | 0 (0.0) | 1 (2.6) | |
| Others | 22/1,205 (1.8) | 12/1,145 (1.0) | 3 (14.3) | 7 (17.9) | |
| Indication for ICD | | | | | |
| Secondary prevention | 340/655 (51.9) | - | 273/429 (63.6) | 67/226 (29.6) | - |
| Primary prevention | 315/655 (48.1) | - | 156/429 (36.4) | 159/226 (70.4) | |
| Baseline heart disease | | | | | |
| None | 961/1,786 (53.8) | 961/1,132 (84.9) | - | - | - |
| IHD | 231/1,786 (12.9) | 80/1,132 (7.1) | 112/429 (26.1) | 39/225 (17.3) | |
| DCM | 169/1,786 (9.5) | 7/1,132 (0.6) | 39/429 (9.1) | 123/225 (54.7) | |
| Brugada syndrome | 81/1,786 (4.5) | 0/1,132 (0.0) | 81/429 (18.9) | 0/225 (0.0) | |
| HCM | 82/1,786 (4.6) | 18/1,132 (1.6) | 61/429 (14.2) | 3/225 (1.3) | |
| Cardiac sarcoidosis | 62/1,786 (3.5) | 11/1,132 (1.0) | 27/429 (6.3) | 24/225 (10.7) | |
| IVF | 39/1,786 (2.2) | 0/1,132 (0.0) | 39/429 (9.1) | 0/225 (0.0) | |
| DHCM | 25/1,786 (1.4) | 0/1,132 (0.0) | 9/429 (2.1) | 16/227 (7.1) | |
| ARVC | 17/1,786 (1.0) | 0/1,132 (0.0) | 15/429 (3.5) | 2/227 (0.9) | |
| Others | 119/1,786 (6.7) | 55/1,132 (4.9) | 46/429 (10.7) | 18/227 (8.0) | |
| With atrial lead | 1,586 (85.8) | 976 (83.6) | 378 (85.3) | 232 (97.5) | <0.0001[a] |
| EF | 57.7±16.2, n=1,775 | 64.2±9.8, n=1,108 | 54.8±16.5, n=434 | 32.2±13.2, n=233 | <0.0001[b] |
| N of Transmission | 9.0±9.2 | 6.5±6.2 | 13.3±12.1 | 12.7±11.1 | <0.0001[b] |
| Follow up periods (days) | 774.9±652.9 | 670.2±605.3 | 1,006.6±731.0 | 857.5±602.0 | <0.0001[b] |
| Device Company | | | | | |
| Medtronic | 860 (46.5) | 421 (36.0) | 268 (60.5) | 171 (71.8) | <0.0001[a] |
| Biotronik | 709 (38.3) | 586 (50.2) | 100 (22.6) | 23 (9.7) | |
| Abbot Medical | 182 (9.8) | 142 (12.2) | 15 (3.4) | 25 (10.5) | |
| Boston Scientific | 98 (5.3) | 19 (1.6) | 60 (13.5) | 19 (8.0) | |

Values are the mean±standard deviation or number (%) of patients. The sum of the percentages may not equal 100% because of rounding.

[a]p values were calculated using Pearson's chi-square test.

[b]p values were calculated using the Kruskal-Wallis test.

PM: pacemaker, ICD: implantable cardioverter defibrillator, CRT-D: cardiac resynchronization therapy defibrillator, AVB: atrioventricular block, SSS: sick sinus syndrome, AF: atrial fibrillation, IHD: ischemic heart disease, DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, DHCM: dilated phase hypertrophic cardiomyopathy, IVF: idiopathic ventricular fibrillation, ARVC: arrhythmogenic right ventricular cardiomyopathy, EF: ejection fraction

5.0%; CRT-D, 5.9%) (Table 2). Battery depletion events included premature triggering of the elective replacement indicator in 7 Enrhythm (Medtronic) devices and one unexpected battery depletion in an ICD. With the exception of ICD therapy, there were no significant differences in the critical events among the three groups.

In the multivariate analysis to assess the risk of critical events, the independent risk factors for critical events were ICD (ICD vs. PM: odds ratio, 7.895; 95% confidence interval, 3.360-18.553; p<0.0001), CRT-D (CRT-D vs. PM, odds ratio, 5.519; 95% confidence interval, 2.249-13.548; p=0.0002), and low ejection fraction (odds ratio, 0.986; 95% confidence interval, 0.973-0.998; p=0.0232). Age, sex, baseline heart disease, and CIED manufacturer were not independent risk factors for critical events (Table 3).

In the multivariate analysis, the risk factors for critical events in the PM and CRT-D groups could not be analyzed due to the low number of critical events. In patients with ICDs, the independent risk factors for critical events included old age, low ejection fraction, Brugada syndrome, dilated phase hypertrophic cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy rather than ischemic heart disease (Table 4).

## Discussion

### Main findings

The main finding of this retrospective cohort study was that the critical event rate was very low, although abnormal events were identified in approximately two-thirds of all data transmissions. In addition, the critical event rate in PM

**Table 2. Transmission Data Characteristics by Devices.**

| Variable | Overall | PM | ICD | CRT-D | p value[b] |
|---|---|---|---|---|---|
| Number of transmission | 16,565 | 7,634 | 5,911 | 3,015 | - |
| Abnormal event | | | | | |
| Overall | 11,040 (66.7) | 4,626 (60.6) | 3,900 (66.0) | 2,514 (83.4) | <0.0001 |
| ATA | 5,981 (36.1) | 3,317 (43.5) | 1,423 (24.1) | 1,241 (41.2) | <0.0001 |
| VTA | 3,753 (22.7) | 1,392 (18.2) | 1,423 (24.1) | 938 (31.1) | <0.0001 |
| Abnormal battery voltage event[a] | 334 (2.0) | 55 (0.7) | 180 (3.0) | 99 (3.3) | <0.0001 |
| Critical event | | | | | |
| Overall | 676 (4.1) | 66 (0.9) | 390 (6.6) | 220 (7.3) | <0.0001 |
| Battery depletion | 19 (0.1) | 7 (0.1) | 8 (0.1) | 4 (0.1) | - |
| ICD therapy | 476 (2.9) | - | 298 (5.0) | 178 (5.9) | - |
| Appropriate therapy | 374/465 (80.4) | - | 239/292 (81.8) | 135/173 (78.0) | - |
| Inappropriate therapy | 91/465 (19.6) | - | 53/292 (18.2) | 38/173 (22.0) | - |
| Lead impedance abnormality | 36 (0.2) | 19 (0.2) | 13 (0.2) | 4 (0.1) | - |
| Non-physiologic noise | 86 (0.5) | 24 (0.3) | 42 (0.7) | 20 (0.7) | - |
| Sensing failure | 11 (0.1) | 6 (0.1) | 3 (0.1) | 2 (0.1) | - |
| Pacing failure | 6 (0.0) | 6 (0.1) | 0 (0.0) | 0 (0.0) | - |
| Acute reduced atrial or ventricular sensing | 5 (0.0) | 3 (0.0) | 1 (0.0) | 1 (0.0) | - |
| Acute increased atrial or ventricular pacing threshold | 31 (0.2) | 6 (0.1) | 17 (0.3) | 8 (0.3) | - |
| Sustained VT out of therapy zone | 19 (0.1) | - | 10 (0.2) | 9 (0.3) | - |
| Others | 11 (0.1) | 0 (0.0) | 8 (0.1) | 3 (0.1) | - |

Values are the number (%) of patients. The sum of the percentages may not equal 100% because of rounding.

[a]Six missing data were excluded from the analysis.

[b]p values were calculated using a generalized estimating equation with a compound symmetry working correlation structure that accounted for associations between repeated measures within subjects.

PM: pacemaker, ICD: implantable cardioverter defibrillator, CRTD: cardiac resynchronization therapy defibrillator, ATA: atrial tachyarrhythmia, VTA: ventricular tachyarrhythmia

**Table 3. Multivariate Analysis to Estimate the Correlations of Critical Events with Covariates.**

| Variable (Definition of Odds Ratio) | Odds Ratio [95% CI] | p value |
|---|---|---|
| Age | 1.008 [0.997-1.020] | 0.1487 |
| Gender (Female/Male) | 0.705 [0.490-1.015] | 0.0604 |
| Device (ICD/PM) | 7.895 [3.360-18.553] | <0.0001 |
| Device (CRT-D/PM) | 5.519 [2.249-13.548] | 0.0002 |
| Company (B/A) | 1.002 [0.707-1.420] | 0.9905 |
| Company (C/A) | 1.161 [0.694-1.943] | 0.5692 |
| Company (D/A) | 1.418 [0.822-2.444] | 0.2090 |
| Baseline heart disease (IHD/None) | 0.490 [0.201-1.197] | 0.1178 |
| Baseline heart disease (DCM/None) | 0.968 [0.385-2.432] | 0.9448 |
| Baseline heart disease (Brugada syndrome/None) | 0.932 [0.338-2.569] | 0.8920 |
| Baseline heart disease (HCM/None) | 0.693 [0.240-1.999] | 0.4978 |
| Baseline heart disease (Cardiac sarcoidosis/None) | 0.884 [0.336-2.324] | 0.8027 |
| Baseline heart disease (IVF/None) | 0.864 [0.295-2.535] | 0.7903 |
| Baseline heart disease (DHCM/None) | 1.526 [0.429-5.425] | 0.5140 |
| Baseline heart disease (ARVC/None) | 1.648 [0.555-4.895] | 0.3682 |
| Baseline heart disease (Others/None) | 0.845 [0.351-2.035] | 0.7074 |
| Atrial lead (With/Without) | 1.227 [0.755-1.994] | 0.4078 |
| EF | 0.986 [0.973-0.998] | 0.0232 |

Company A, B, C and D indicated Medtronic, Biotronik, Abbot Medical and Boston Scientific, respectively.

CI: confidence interval, PM: pacemaker, ICD: implantable cardioverter defibrillator, CRT-D: cardiac resynchronization therapy defibrillator, IHD: ischemic heart disease, DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, DHCM: dilated phase hypertrophic cardiomyopathy, IVF: idiopathic ventricular fibrillation, ARVC: arrhythmogenic right ventricular cardiomyopathy, EF: ejection fraction

**Table 4. Multivariate Analysis to Estimate the Factors Correlated with Critical Events in Patients with ICDs.**

| Variable (Definition of Odds Ratio) | Odds Ratio [95% CI] | p value |
|---|---|---|
| Age | 1.017 [1.003-1.031] | 0.0183 |
| Gender (Female/Male) | 0.690 [0.395-1.204] | 0.1910 |
| Company (B/A) | 1.136 [0.714-1.808] | 0.5898 |
| Company (C/A) | 1.855 [0.596-5.772] | 0.2861 |
| Company (D/A) | 1.428 [0.705-2.893] | 0.3231 |
| Baseline heart disease (DCM/IHD) | 1.073 [0.534-2.160] | 0.8424 |
| Baseline heart disease (Brugada syndrome/IHD) | 2.323 [1.099-4.912] | 0.0274 |
| Baseline heart disease (HCM/IHD) | 1.631 [0.713-3.730] | 0.2462 |
| Baseline heart disease (Cardiac sarcoidosis/IHD) | 1.864 [0.812-4.278] | 0.1418 |
| Baseline heart disease (IVF/IHD) | 2.254 [0.951-5.342] | 0.0649 |
| Baseline heart disease (DHCM/IHD) | 5.579 [1.441-21.604] | 0.0128 |
| Baseline heart disease (ARVC/IHD) | 4.125 [1.772-9.604] | 0.0010 |
| Baseline heart disease (Others/IHD) | 2.519 [1.187-5.347] | 0.0161 |
| EF | 0.978 [0.963-0.994] | 0.0080 |
| Indication for ICD (Primary/Secondary) | 1.031 [0.665-1.598] | 0.8918 |

Company A, B, C and D indicated Medtronic, Biotronik, Abbot Medical and Boston Scientific, respectively.

CI: confidence interval, PM: pacemaker, ICD: implantable cardioverter defibrillator, CRT-D: cardiac resynchronization therapy defibrillator, IHD: ischemic heart disease, DCM: dilated cardiomyopathy, HCM: hypertrophic cardiomyopathy, DHCM: dilated phase hypertrophic cardiomyopathy, IVF: idiopathic ventricular fibrillation, ARVC: arrhythmogenic right ventricular cardiomyopathy, EF: ejection fraction

patients was significantly lower than that in ICD or CRT-D patients. The patients with a low ejection fraction were likely to have critical events. The expert consensus statement proposed in-hospital visits every 6-12 months for patients with PM. If the selection of patients for CIED follow-up could be limited to those who have experienced a critical event, the workload would decrease dramatically. This study is the first report to examine the factors, including devices made by various manufacturers and types of CIEDs, associated with high critical event rates in "real-world" CIED patients.

### Definitions of critical events

The critical events are defined in the Methods. ATA events that required anticoagulation therapy and heart failure-related events were excluded because the strategy for intervention was not indicated, which led to a large difference in the intervention rate that was dependent on physicians. Recent CIEDs have many parameters that require precise tuning, such as AV delay, VV delay, refractory period, blanking period, pacing mode, rate response, automatic pacing threshold testing, and automatic sensitivity setting, which also showed a major difference in the intervention rate that was dependent on the physician. Although these data might have been related to the clinical intervention rate, this study only focused on critical events that definitely required intervention. Thus, the critical event rate in the present study might have been underestimated.

### The critical event rate in previous reports

As reported by Facchin et al. (16), the critical event rate was very low in the PM population. They reported that 1,882 (38%) patients had at least one clinically relevant event that required further investigation among a total of 4,965 remote transmissions; however, only 137 interventions (2.8%) were required after further investigation by expert nurses and doctors. Their critical event rate was slightly higher than that in the present study because AF events were excluded from critical events. Ricci et al. (17) also reported that 133 (6%) patients consulted a physician for further clinical evaluation, and 55 (2%) required additional intervention to restore transmission interruption of the 2,249 analyses performed by nurses, which was similar to the present results. However, the types of CIEDs in the population, which included PM, ICD, and CRT-D patients, were not analyzed.

In the present study, patients with a low ejection fraction were likely to have critical events, which was in accordance with previous reports. As previously reported, patients with a low ejection fraction were likely to have appropriate ICD therapies (18-20), which was closely associated with critical events.

Several studies have analyzed the transmitted data of different types of CIEDs. Lazarus (21) reported that the mean numbers of events per patient per month reported by Home Monitoring to caregivers were 1.1, 0.7, and 2.1 (overall average, 0.6), for PM, ICD, and CRT-D recipients, respectively. In the ATHENS multicenter registry (22), the preva-

lence of "visit with action" (corresponding to the present "critical event") in the PM, ICD, and CRT groups was 22.8%, 18.6%, and 29.8%, respectively. In these studies, the event rate was lowest in the ICD group, but the definition of critical event was different from that of the present study. The patient characteristics, patient population, and the underlying diseases of the enrolled patients could account for the differences between our study and these previous studies.

The present study showed that the critical event rate did not differ according to device manufacturer. This result could imply that the RM system would be effective in managing the follow-up of CIED patients, regardless of the device manufacturer. de Ruvo et al. (23) compared daily RM transmission systems (BHM) to periodic RM transmission systems (BSL, MCL, and AMM) and noted that daily transmission was associated with a higher cumulative rate of actionable events. In the present study, the proportion of ICD patients with BHM was relatively low, while that of PM patients with BHM was relatively high. In addition to the different definitions of critical events, this fact might have affected the present results..

In the ECOST trial (24), RM of ICD patients reduced costs, reducing the scheduled or additional ambulatory device evaluations per patient-year in an RM follow-up group in comparison to a conventional follow-up group. Although the present study did not show the cost-effectiveness of RM follow-up, the low critical event rate might lead to indirect cost savings.

In the ICD group, independent risk factors for critical events included Brugada syndrome, dilated phase hypertrophic cardiomyopathy, and arrhythmogenic right ventricular cardiomyopathy rather than ischemic heart disease. In patients with Brugada syndrome, it is reported that in addition to ICD therapy, adverse events, such as inappropriate ICD therapy, lead failure, or infection often occurred (25, 26). In patients with arrhythmogenic right ventricular cardiomyopathy, it is also reported that critical events associated with ICD are likely to occur (27, 28). However, no previous reports have compared the critical event rates among these groups.

### Limitations

The present study was associated with some limitations. First, it was a multicenter, retrospective study that included a moderately sized study population. A prospective study with a larger study population could increase the reliability of these results. Second, only transmitted data and limited patient background data were analyzed in this study, whereas other data, such as comorbidities, the prognosis, and medications, were not evaluated, which have revealed other categories that should receive attention. Third, the frequency of transmissions differed among hospitals and manufacturers, which might have affected the critical event rate. However, the transmission interval was within the recommended values of between 1 and 4 months; thus, we consider that a reliable database was maintained. Fourth, in the present study, only data transmitted by RM were analyzed, real intervention events in the outpatient clinic were not. Thus, the real intervention rate may differ from the critical event rate of the present study. Lastly, the device programming and management was non-standardized, which might have also influenced the critical event rate. However, the data in this study shows "real-world" results.

## Conclusion

Although abnormal events were observed in approximately two-thirds of all transmitted RM data, the critical event rate was <1% in the PM group, which was lower in comparison to the ICD and CRT-D groups. A low ejection fraction was an independent predictor of critical events. If the selection of patients with CIEDs for follow-up could be limited to those with critical events, the workload would decrease dramatically.

**The authors state that they have no Conflict of Interest (COI).**

**Acknowledgement**

The authors thank Motomi Tachibana, MD, PhD, Kohei Miyaji, MD, PhD, Shigeki Hiramatsu, MD, PhD, Akira Ueoka, MD, Keisuke Okawa, MD, Etsuko Ikeda, MD, Takefumi Oka, MD, PhD, Kenji Kawamoto, MD, Tadashi Wada, MD, PhD, Shingo Hosogi, MD, PhD, Mika Nishimoto, MD, PhD, Masamichi Tanaka, MD, PhD, Chisato Suezawa, MD, PhD, Sho Tsushima, MD, Kenki Enko, MD, PhD, Yasufumi Kijima, MD, PhD, Toru Miyoshi, MD, PhD, and Tohru Ohe, MD, PhD. The authors also thank Hirotaka Iguchi, Norihiro Nishiyama, Yuki Takenaka, Katsuaki Sakate, and Susumu Iwado for the medical engineering work and Yuko Kobayashi, Miyuki Fujiwara, and Masayo Ohmori for the secretarial work.

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