Reliability of Implantable Cardioverter Defibrillator
Home Monitoring in Forecasting the Need for Regular Office Visits, and Patient Perspective
– Japanese HOME-ICD Study –
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**Background:** Remote monitoring (RM) technology has emerged as a potentially efficient method to manage patients with implantable cardioverter defibrillators (ICDs) or cardiac resynchronization therapy defibrillators (CRT-Ds). This study evaluated the reliability of daily RM in forecasting the need for regular in-hospital follow-ups (RFUs).

**Methods and Results:** Two hundred and fifteen patients implanted with Biotronik Lumax devices (142 ICDs, 73 CRT-Ds) were enrolled. RFU was performed at 3, 6, 9, and 12 months after implantation. Immediately before an RFU, the physician forecasted the need for RFU based on RM data (pre-RFU assessment). A completed RFU session was classified as necessary if an action was undertaken potentially influencing patient safety, device therapy, or medication therapy (post-RFU assessment). Overall, 663 pairs of pre- and post-RFU assessments were compared. The number of pre-RFU assessments failing to predict the need for RFU was 38 (5.7%), fulfilling the study hypothesis of 5.0±4.0% (P<0.002; 95% confidence interval: 4.1–7.8%). Judged by an independent committee, the rate of false pre-RFU forecasts with high clinical relevance was 2 (0.3%). RM correctly forecasted non-necessity of 498 scheduled RFUs (75.1%). Patient acceptance of RM was evaluated using a targeted questionnaire. Of 182 interviewed patients, 172 (94.5%) felt security and comfort.

**Conclusions:** RM-based forecasts appear sufficiently accurate to safely individualize RFU. Most patients have a positive attitude towards RM. (Circ J 2013; 77: 2704–2711)

**Key Words:** Cardiac resynchronization therapy defibrillator; Implantable cardioverter defibrillator; Patient-centered care; Remote monitoring; Telemedicine

The evolving telemonitoring capabilities of implantable cardioverter defibrillators (ICDs) and cardiac resynchronization therapy defibrillators (CRT-Ds) allow remote evaluation of multiple parameters related to the device function and cardiovascular physiology. Information can travel to the physician as often as needed rather than being dependent on the patient traveling, potentially enabling tailored follow-up and a highly individualized medical management in a way that has never been possible before. Without remote monitoring (RM), the ICD and CRT-D recipients typically undergo clinical checks every 3–6 months. Most of these routine checks involve device interrogation and do not elicit any changes in the device’s programming or patient’s therapy. If clinic visits without an action can be skipped based on RM data, the in-office follow-up burden will be reduced significantly for both hospitals and patients.

In the Biotronik Home Monitoring® system (Berlin, Germany), subsequently referred to as “Home Monitoring,” data transmission occurs automatically once a day and additionally on detection of a clinical or technical anomaly. Given that only some of the data stored in the implant’s mem-

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Reliability of ICD Home Monitoring

Criteria were: (1) contraindication for ICD or CRT-D therapy; (2) a medical condition or geographical instability likely to prevent regular follow-up attendance; (3) inability to handle the Home Monitoring system; (4) living in an area with insufficient 3G mobile phone coverage; or (5) participation in another clinical study.

Home Monitoring

The implantation and patient discharge procedures were performed according to institutional standards. After patient discharge, the following data were transmitted daily via the Home Monitoring function in a patient-independent manner: counts of arrhythmia episodes; counts of initiated and successful or unsuccessful ICD therapies combined with high-resolution intracardiac electrograms; rhythm information (eg, prevalence of pacing/sensing, atrial fibrillation burden); and technical parameters, such as lead or shock impedance, right and left ventricular pacing thresholds, and battery status.

Additional data transmissions could occur automatically upon detection of arrhythmia episodes or technical anomalies. Data sent by the implanted device were received by a Home Monitoring patient device capable of automatically relaying the data to the Biotronik Home Monitoring Service Center (Berlin, Germany) over a 3G mobile phone network. After automated analysis at the service center, the data were posted on a secure internet site accessible to the physician responsible for the patient’s care.

Regular Follow-ups

Regular in-hospital follow-up examinations were scheduled for 3, 6, 9, and 12 months after implantation, to perform standard ICD or CRT-D follow-up. The treating physicians also documented reasons for device reprogramming, specified current medication therapy and reasons for any changes, and evaluated the patient’s acceptance of Home Monitoring on a targeted questionnaire.

Methods

This prospective, non-randomized study was conducted at 41 investigational sites in Japan (Data S1). The ethics committee in each institution approved the study protocol. All patients provided written informed consent. The investigation was conducted according to the Japanese Guidelines for Clinical Studies and the Declaration of Helsinki.

Patient Selection

To be enrolled, patients had to: (1) have an indication for ICD or CRT-D implantation according to the ACC/AHA/HRS 2008 Guidelines for Device-based Therapy of Cardiac Rhythm Abnormalities; (2) be fitted with an ICD or a CRT-D from the Lumax family (Biotronik, Berlin, Germany); and (3) be able to comply with the study protocol. Patient exclusion criteria were: (1) contraindication for ICD or CRT-D therapy; (2) a medical condition or geographical instability likely to prevent regular follow-up attendance; (3) inability to handle the Home Monitoring system; (4) living in an area with insufficient 3G mobile phone coverage; or (5) participation in another clinical study.

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Data Evaluation and Study Objectives

The primary objective was to evaluate the reliability of Home Monitoring technology in predicting the need for regular in-hospital follow-ups. To this end, the pre- and post-follow-up assessments for regular visits were compared to derive the rate of true and false predictions using the scheme shown in Figure 1B. In particular, false-negative predictions (an action undertaken during a follow-up visit contrary to the forecast by the physician) were the focus of the present research, and are described in detail. An example of false-negative prediction is when the ventricular pacing output is increased at an office visit to maintain adequate safety margin or when the output is decreased to extend battery longevity, and this reprogramming was not anticipated based on Home Monitoring data because the implanted device did not transmit pacing threshold values.

All cases of false-negative predictions were scrutinized for

Forecasting of Follow-up Necessity by Home Monitoring

Figure 1A summarizes physician activities related to regular in-hospital follow-up. At 0–3 days before regular follow-up, the treating physician assessed the need for hospital visit based on the cumulated Home Monitoring data (pre-follow-up assessment). If there appeared to be a need to change medication, modify ICD or CRT-D programming, revise the implanted system, or conduct an additional examination (eg, stress electrocardiogram or long-term electrocardiogram), the follow-up visit was forecasted as necessary.

After completion of a regular follow-up, the treating physician provided the post-follow-up judgment on the need for this follow-up, which was classified as necessary if an action was undertaken potentially influencing patient safety, device therapy, or medication therapy.
The sample size of the study was based on the primary study hypothesis. For a 2-sided significance level of 5% (α) and a statistical power of 90% (1-β), a minimum sample of 442 regular in-hospital follow-ups was needed. Assuming a follow-up attrition rate of up to 30%, 10 158 patients were sufficient. The study met this enrolment objective.

To analyze primary and secondary study hypotheses, the Pearson-Clopper 95% CIs were calculated. Because multiple events were possible in a patient, the CI for the primary study hypothesis was corrected with the generalized equation estimation (GEE) method, where the best fit model using logit link function was achieved with an autoregressive AR (1) correlation matrix.

For continuous data, means, standard deviation, and/or medians were calculated and, for categorical data, the absolute and relative frequencies. Study results were compared for ICD and CRT-D patients using a 2-sided t-test (for normally distributed continuous data), Mann-Whitney-U test or Wilcoxon test (non-normally distributed continuous data and ordinal data), or a chi-squared test according to Pearson’s or Fisher’s exact test as appropriate (categorical data). In all cases, statistical significance was set at P<0.05. Analysis was conducted using IBM SPSS 20 for Windows (IBM, Armonk, NY, USA).

Results

Between May 2009 and August 2010, 215 patients were enrolled in the study (Table 1). One-third of them underwent a prophylactic ICD implantation. Most patients received a dual-chamber ICD (n=117), and the rest were fitted with a single-chamber ICD (n=25) or a CRT-D (n=73). At baseline, ICD and CRT-D patients differed significantly in many parameters: CRT-D recipients were older, had more frequent cardiomyopathy, lower ejection fraction, greater use of β-blocker therapy, and longer QRS duration than ICD recipients.

The mean follow-up duration was 332±103 days (median, 366 days) for the 215 patients, including 11 patients who withdrew from the study before the first regular follow-up visit.
Reliability of Forecasts

The number of complete pairs of pre- and post-follow-up assessments was 667 (96.8%), out of 689 documented regular in-hospital follow-ups. Four of these forecasts were excluded from the final analysis because they were given after the upgrade from an ICD to a CRT-D system in 2 patients. The distribution of 663 contributing forecasts per 3/6/9/12-month follow-up point was 173/167/160/163, respectively.

The rate of false-negative forecasts of 5.7% (38 cases out of 663) was significantly lower than the hypothesized upper limit of 9.0% (P<0.002; Pearson-Clopper 95% CI: 4.1–7.8%; GEE-corrected 95% CI: 4.2–7.7%; Table 2, Figure 3). Hence, the primary study hypothesis was fulfilled. False-negative forecasts were significantly more frequent in the CRT-D group (8.3% vs. 4.5%; P<0.05). There was no difference in the rate of false-negative forecasts between men and women.

The Clinical Relevance Committee scrutinized all 38 false-negative forecasts and judged 36 of them to be non-critical and 2 (0.3% of all 663 forecasts) to have high clinical relevance (Table 2). Of the 36 non-critical false-negative forecasts, 13 were caused by physician oversight (ie, suboptimal programming of the tachyarrhythmia detection zones, T-wave oversensing, episodes of arrhythmias requiring medication change, ventricular pacing threshold changes, low sensing amplitudes, and an unnecessarily high percentage of right ventricular pacing). The distribution of the 38 false-negative forecasts per 3/6/9/12-month follow-up point was 16/9/5/8, respectively.

Home Monitoring permitted reliable prediction of unnecessary office visits in 498 regular follow-ups (75.1%, true negative; Figure 3). It also reliably predicted necessary office visits, requiring changes in device or medication therapy, in 74 regular follow-ups (11.2%, true positive). In contrast, no changes in device or medication therapy were undertaken at 53 false-positively forecasted regular follow-ups (8.0%). Not only remarkable arrhythmia or other data transmitted by Home Monitoring were stated as follow-up reasons in these 53 cases, but also patient hospitalization since the last follow-up (n=15), known problems with the implanted leads (n=3), and cardiovascular symptoms reported by the patient (n=1). Overall, 83.1% of regular follow-ups were not contributory, calculated as true negative (75.1%)+false positive (8.0%).

Time Gain for Silent Events

After exclusion of 10 silent events occurring after ICD to CRT-D system upgrade in 2 patients, 830 silent events in 83 patients were considered. The number of, and an estimated time gain for, different event types are summarized in Figure 4. The estimated time gain for all events (mean, 40.5±29.2 days; median, 37.0 days) was significantly greater than the hypothesized 30 days (P<0.001; 95% CI: 38.3–42.7 days). Hence, the secondary study hypothesis was fulfilled.

Patient Perspective on Home Monitoring

The completed questionnaire was obtained from 182 patients (84.7%) at 326±91 days after implantation. Only 5.5% of interviewed patients had no improved feeling of security and 3.3% had no improved feeling of comfort due to regular data transfer (Figure 5). The majority of patients never worried about the Home Monitoring device (92.9%) and never found it a bother to have the device at home (92.3%). For 96.2%, the Home Monitoring device was not a nuisance.

Major Adverse Events

A total of 12 patients died from cardiac (n=3), non-cardiac (n=8), or unknown (n=1) causes. The severe device-related adverse events consisted of surgical revisions to treat pocket infection (n=2), ICD lead dislodgment (n=3), or left ventricular lead dislodgment (n=2), as well as inappropriate shock therapy caused by atrial fibrillation (n=5, in 3 patients), T-wave oversensing (n=1), and external electrical muscle stimulation (n=1). One myocardial infarction was reported, but no case of stroke.

Discussion

The number of patients treated with an ICD or a CRT-D is steadily increasing. Recently, CRT-D therapy was shown to be equally effective in Japanese as in Western patients, even if pre-identification of CRT responders still represents a significant challenge. The growing use of implantable cardiovascular electronic devices translates into an increasingly heavy workload for physicians in charge of regular follow-up. Remote follow-up option is becoming increasingly attractive as a substitute for clinic visits, despite some unsolved safety, legal, and reimbursement issues. It is important to clarify whether cumulative Home Monitoring data allow reliable assessment of the need for routine office visits as would be necessary to implement the concept of individualized follow-up schedule.
Figure 4. Time gain in the diagnosis of silent events by Home Monitoring. Data given as median with interquartile range, and minimum and maximum. Device events were defined as special implant status (inactive detection of ventricular tachyarrhythmia); none of the events was associated with lead impedance, shock impedance, or battery status. *P<0.05 for ICD vs. CRT-D groups. CRT-D, cardiac resynchronization therapy defibrillator; ICD, implantable cardioverter defibrillator.

Figure 5. Distribution of patient answers in the questionnaire from Figure 2. Security/comfort: 1, very much so; 2, somewhat; 3, not at all; worry/bother: 1, never; 2, sometimes; 3, very often; nuisance: 1, not at all; 2, somewhat; 3, very much so. There were no statistically significant differences between the ICD and CRT-D groups. CRT-D, cardiac resynchronization therapy defibrillator; ICD, implantable cardioverter defibrillator.
Study Findings
The low rate of false-negative forecasts (5.7%) and the substantial temporal gain in the diagnosis of silent events (median, 37 days) fulfilled primary and secondary study hypotheses. Only 2 false-negative forecasts were judged post-hoc to be of high clinical relevance (0.3% of all forecasts), whereas others appeared to be non-critical.

Prior to the present study, only the HOME-ICD study of 271 ICD patients followed for 12 months systematically evaluated the proportion of false-negative forecasts based on Home Monitoring, and found it to be 14.2% (of 908 forecasts). This considerably higher rate of false-negative forecasts was partly attributable to the use of older-generation devices incapable of transmitting intracardiac electrograms or pacing thresholds. In the present study, including both ICD and CRT-D recipients, 5.7% of all forecasts (or 4.5% of ICD-related forecasts) were false negative, which represents a remarkable improvement. Furthermore, 13 of 38 false-negative forecasts occurred because of incorrect interpretation of Home Monitoring data by clinical investigators, signifying the need for better training programs. Also, 7 other false-negative forecasts were due to unavailability of pacing threshold transmissions in the second-newest device family (Lumax 340), a problem now resolved with Lumax 540. Without these 2 problems, the number of false-negative forecasts would be 18 (2.7%). Both false-negative events judged as clinically highly relevant, however, could have been detected by a general practitioner. RM does not negate clinical follow-up by a non-electrophysiologist.

In the literature, the proportion of “contributory” or “actionable” follow-ups, approximately defined as a visit prompting a change in patient management or device reprogramming, in conventionally followed pacemaker, ICD, or CRT(-D) patients, ranges from 7% to 50%, depending on the exact definition of contributory follow-ups. 

The vast majority of patients have a positive attitude and experience with Home Monitoring, which is not unique to this remote technology. A minority of—mostly elderly—patients, however, do not accept remote monitoring, primarily because of fear of technology or concerns about privacy or about the risk of losing contact with nurses and physicians. Eleven patients (5.1%), thus, withdrew early from the present study. Of those continuing in the study, only a few (3.3–7.7%) did not feel that security and comfort had improved or had some worries or were bothered about Home Monitoring. By comparison, in a recent survey of 1,109 pacemaker, ICD, and CRT(-D) patients undergoing conventional face-to-face follow-up practice, every third patient perceived such practice as bothersome and approximately 90% of patients had a favorable opinion on the RM concept proposed.

Study Limitations
Only patients living in Japan were recruited, and the need to evaluate other ethnic groups remains. A larger patient group could increase the accuracy of study findings. The study was not designed to measure and compare the time saved through fewer face-to-face encounters and the time required for regular Home Monitoring data evaluation. The present results may not be extrapolated to other RM systems. Alternative systems do not transmit data automatically every day, which may result in different time gain and reliability of event detection and in a different patient perspective on the security and comfort of the RM system.

Conclusions
The reliability of daily, automated RM in forecasting the need for in-hospital follow-ups appeared to be sufficiently accurate to safely individualize in-hospital patient evaluations in the future and so avoid unnecessary hospital visits. Aside from the technical reliability, human errors were indicated in data interpretation. Patient medical management in some cases may render data retrieved from the implanted devices insufficient to substitute in-hospital follow-ups completely. The vast majority of patients had a positive response to the Home Monitoring system at home.

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