Follow-Up of CRT-ICD: Implications for the Use of Remote Follow-Up Systems. Data from the InSync ICD Italian Registry

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Background: Launch of remote follow-up systems in Europe is currently underway. However, there is insufficient understanding of postimplant practices with respect to device follow-up, reprogramming of device features, and postshock clinic visits.

Methods: We analyzed device-stored data from patients implanted with biventricular defibrillators (CRT-ICD) to characterize the management of patients in current clinical practice and the potential impact of remote follow-up systems.

Results: Two hundred and seventeen patients were identified, all with complete device-data for at least one year. Over a follow-up period of 570 ± 158 days, 1,959 device interrogations were performed. Of these, the majority (1,280, 65%) involved the reprogramming of device parameters. The mean time interval between interrogations was 70 ± 25 days. Overall, a marked reduction of interrogations requiring reprogramming was observed between the first six months of follow-up and subsequent periods (from 3.6 ± 1.8 to 1.1 ± 1.0 interrogations/six months). A mean of 6.0 ± 5.9 device parameters was reprogrammed during the first six months of follow-up, versus 4.4 ± 5.6 (P = 0.000) during the subsequent period. From multivariate analysis, a higher-than-median number of interrogations was found to be significantly associated with defibrillator shocks (OR:2.51; 95%CI:1.42–4.42). Following a shock, a total of 133 interrogations in 60 patients were performed with 80% of these occurring within five days of the shock, and 49% did not require device reprogramming.

Conclusion: Six months after implant, reprogramming of device parameters is significantly less frequent, making the use of remote follow-up systems a practical alternative for patients and physicians. Moreover, a considerable portion of post-shock interrogations does not involve reprogramming and may therefore be performed remotely. (PACE 2008; 31:38–46)

Introduction

The efficacy of implantable cardioverter-defibrillators (ICD) for primary or secondary prevention of sudden cardiac death in patients with ischemic or nonischemic cardiomyopathy has been shown in several large-scale randomized trials.1–6 Similarly, cardiac resynchronization therapy (CRT) alone or associated with ICD has been demonstrated to reduce all-cause mortality.7,8 Consequently, the ICD and CRT indications have been expanded9,10 and this has led to a rise of device implantations worldwide.11

Currently, outpatient follow-up of ICD patients are scheduled in regular three to six month intervals and for acute events like symptoms or shocks. The growing demand for implantable device follow-up poses a challenge to implanting physicians, technicians, and nurses in the ICD clinic.12,13 In response to that, several major device companies are offering a technology for remote ICD monitoring.14–16 The proposed systems differ in the type of data provided and the manner in which the device data are retrieved and transmitted. However, none of the remote ICD surveillance systems currently allow physicians to remotely reprogram the cardiac device.
Launch of remote follow-up systems in Europe is currently underway to provide remote device interrogations capability. However, there is insufficient understanding of postimplant practices with respect to device follow-up, reprogramming of device features, and postshock clinic visits.

We analyzed device-stored data from patients implanted with CRT-ICD and enrolled in a national observational registry to characterize the management of implanted device patients in clinical practice in Italy and assess the potential impact of remote follow-up systems.

**Methods**

**Data Collection and Analysis**

From 1999 to 2005, patients successfully implanted with biventricular ICD (Medtronic Inc., Minneapolis, MN, USA), were prospectively included in the InSync ICD Italian Registry. The Registry enrolled patients with mild or severe symptomatic chronic heart failure (New York Heart Association [NYHA] class II–IV), an ejection fraction of less than 35%, a wide QRS complex (>130 ms), and an indication to ICD for primary or secondary prevention of sudden cardiac death (according to the absence or presence of previous history of spontaneous sustained ventricular tachyarrhythmias or cardiac arrest). All patients provided written informed consent approved by each hospital’s Ethic Committee.

The devices and the pacing leads were implanted by means of standard techniques.17 Before device implantation, patients underwent baseline evaluation, including demographics and medical history data collection, clinical examination, 12-lead electrocardiogram, estimation of NYHA functional class, and echocardiographic recording. The modified biplane Simpson’s technique was used to determine the ejection fraction.18 Echo-directed adjustment of the atroventricular pacing interval was usually done before patients were discharged to optimize hemodynamic function.

After the implant, outpatient routine follow-ups were scheduled according to the clinical practice adopted in each participating center. Additional follow-ups were performed following ICD discharge, clinical events, or patient symptoms, based on clinical evaluation of the attending physician.

At each follow-up visit, the device was interrogated to check the proper functioning as well as to review the arrhythmic episodes detected and treated by the ICD, and the stored data were saved to disk. When necessary, the working parameters of the device were reprogrammed. The frequency of device interrogations and the programming of device features were left to the discretion of the attending physician.

Patients implanted with ICDs capable of long-term data storing (Medtronic InSync Marquis model 7277 and InSync III Marquis model 7279) were included in the analysis if complete save-to-disk data were available for at least 12 months.

The devices provide extensive retrievable diagnostics data, including storage of the date of ICD interrogation and reprogramming, time and characteristics of atrial and ventricular arrhythmias with the therapies delivered for each episode, the daily values of mean heart rate, heart rate variability, and patient activity index, all estimated using algorithms described elsewhere.19 Moreover, the device reports the status of each functioning parameter at the time of interrogation.

In this study we estimated the incidence of device interrogations, evaluated the reprogramming of ICD features, and investigated factors associated with frequent device interrogation.

**Statistical Analysis**

Continuous data were expressed using means values with standard deviation. Categorical data were expressed in percentages. Differences between mean data were compared by a t-test for Gaussian variables, and by Mann-Whitney U or Wilcoxon nonparametric test for non-Gaussian variables for independent or paired samples, respectively. Differences in proportions were compared using a $\chi^2$ analysis.

Logistic univariate and multivariate regression analyses were used to identify predictors of a higher frequency (greater than median value) of interrogation, using several baseline variables and device data collected during follow-up (expressed as mean values of the parameters collected every day). Statistical significance was defined as a P-value < 0.05 to perform the multivariate logistic regression analysis.

A P-value < 0.05 was considered significant for all tests. All statistical analyses were performed using SPSS software (version 12.0, SPSS Inc., Chicago, IL, USA).

**Results**

Two hundred and seventeen patients implanted with InSync Marquis devices and with data stored for more than 12 months were included in the analysis. Table I shows demographics and baseline clinical parameters for the study population. Patients were enrolled from February 2002 to June 2004 and followed in 23 implanting centers participating in the InSync ICD Italian Registry. In these institutions different approaches were adopted for routine follow-up visits of CRT-ICD patients: for 70 patients the scheduled
frequency of routine follow-up was four visits per year, while for the remaining 147 patients two visits per year were scheduled.

The mean follow-up duration was $570 \pm 158$ days. For the full study cohort, 123,608 days of device-retrieved data were analyzed.

The data collected by the devices revealed the occurrence of 2,022 episodes of arrhythmias classified by the ICD as ventricular tachycardia or ventricular fibrillation. Of these, 177 episodes were treated with shock therapy, as per the programmed parameters. In the same time period, the devices reported that 1,959 ICD interrogations were performed. In 1,280 (65%) of these, at least one functioning parameter was reprogrammed. The mean time interval between ICD interrogations was $70 \pm 25$ days.

Figure 1 describes the observed distribution of interrogations, with and without reprogramming, since implant. Soon after the implant (six months) we observed many interrogations that frequently included some device reprogramming.

In order to evaluate the overall need for device parameter adjustment during follow-up, we considered the frequency of device reprogramming. A marked reduction in the frequency of reprogramming was observed after six months of follow-up, from $3.6 \pm 1.8$ to $1.1 \pm 1.0$ reprogramming sessions per six-month period ($P < 0.001$).

Moreover, we compared the status of the ICD parameters at the predischarge visit with the six-month visit, and the six-month visit with values from the last available follow-up (Table II).

For this analysis, 60 main device parameters were considered, excluding minor parameters that usually remain unmodified during the device lifetime. The values considered included 25 parameters for CRT and general pacing delivery (pacing mode and rate, intervals, pulse amplitude and duration, special functions for CRT), 17 variables for the detection of tachyarrhythmias (heart rate cutoffs, counters, detection sensitivity, additional detection criteria), and 18 parameters that define the type of therapy delivered for tachycardia episodes (the complete list of the parameters included in the analysis is reported in Fig. 2).

After six months of follow-up ($182 \pm 61$ days), a mean of only $6.0 \pm 5.9$ parameters out of 60 were changed with respect to the predischarge visit in 86% of the patient population. From the six-month visit to the last one (occurring at mean $385 \pm 173$ days) a mean of $4.4 \pm 5.6$ parameters were modified in 75% of patients.

In particular, the need to reprogram CRT parameters decreased after the first six months in terms of the parameters changed and the number of patients undergoing some device adjustment.
On the contrary, the number of modified “tachycardia detection” parameters seemed to increase together with the number of patients undergoing these device changes. The parameters defining the therapy for tachycardia termination remained approximately unmodified in the majority of patients during the entire follow-up period.
### Table III.
Logistic Univariate and Multivariate Regression Analysis of Factors Predicting a Frequency of Interrogations Higher than 5.4/Year (Median Value)

<table>
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<tr>
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<th>Univariate Analysis</th>
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<td></td>
<td>OR</td>
<td>95% CI</td>
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<td>95% CI</td>
<td>P</td>
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<td>Male gender</td>
<td>0.58</td>
<td>0.20–1.65</td>
<td>0.303</td>
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<tr>
<td>Age</td>
<td>0.99</td>
<td>0.96–1.02</td>
<td>0.446</td>
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<td>Ischemic etiology</td>
<td>1.00</td>
<td>0.56–1.80</td>
<td>1.000</td>
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<td>Primary prevention indications</td>
<td>1.30</td>
<td>0.80–2.70</td>
<td>0.358</td>
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<td>NYHA Class IV</td>
<td>0.95</td>
<td>0.29–3.04</td>
<td>0.925</td>
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<tr>
<td>Ejection fraction</td>
<td>1.00</td>
<td>0.96–1.04</td>
<td>0.928</td>
<td>—</td>
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<tr>
<td>Chronic atrial fibrillation</td>
<td>1.08</td>
<td>0.51–2.26</td>
<td>0.849</td>
<td>—</td>
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<tr>
<td>Preimplant HF hospitalizations</td>
<td>0.54</td>
<td>0.26–1.19</td>
<td>0.125</td>
<td>—</td>
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<tr>
<td>Angioplasty/stenting in medical history</td>
<td>1.24</td>
<td>0.59–2.62</td>
<td>0.569</td>
<td>—</td>
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<tr>
<td>Cardiac surgery in medical history</td>
<td>0.78</td>
<td>0.45–1.37</td>
<td>0.391</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Presence of any comorbidity (renal/metabolic/pulmonary)</td>
<td>1.05</td>
<td>0.57–1.92</td>
<td>0.878</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Number of scheduled follow-up per year</td>
<td>1.11</td>
<td>0.82–1.50</td>
<td>0.501</td>
<td>—</td>
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<tr>
<td>Presence of HF outpatients department in the hospital</td>
<td>1.25</td>
<td>0.70–2.24</td>
<td>0.457</td>
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<td>—</td>
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<tr>
<td>Shock therapies per year</td>
<td>2.28</td>
<td>1.36–3.81</td>
<td>0.002</td>
<td>2.51</td>
<td>1.42–4.42</td>
<td>0.001</td>
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<tr>
<td>Time in atrial arrhythmias</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.341</td>
<td>—</td>
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<tr>
<td>Ventricular rate during atrial arrhythmias</td>
<td>1.01</td>
<td>0.99–1.03</td>
<td>0.265</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Mean day heart rate</td>
<td>1.00</td>
<td>0.97–1.03</td>
<td>0.806</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Mean night heart rate</td>
<td>1.02</td>
<td>0.99–1.06</td>
<td>0.167</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Mean heart rate variability</td>
<td>1.00</td>
<td>0.99–1.01</td>
<td>0.541</td>
<td>—</td>
<td>—</td>
<td>—</td>
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<tr>
<td>Mean patient activity (hour/day)</td>
<td>0.80</td>
<td>0.68–0.95</td>
<td>0.011</td>
<td>0.78</td>
<td>0.65–0.94</td>
<td>0.009</td>
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</table>

In Figure 2, we reported, for each parameter, the percentage of patients with device reprogramming during the two periods of follow-up. The most frequently adjusted parameters were the amplitude of left ventricular pacing pulse together with its duration, the amplitude of the atrial and right ventricular pulses, the lower pacing rate, and the atrioventricular delays (all these parameters were modified in more than 20% of patients).

In order to identify the predictors of higher frequency (greater than median value) of device interrogation, we analyzed several baseline variables and the data collected by the device during the follow-up (mean value of the parameters collected every day) by means of logistic regression (Table III). The number of shocks delivered and reduced patient activity are associated with a higher number of interrogations during follow-up.

In our population, 133 interrogations were performed in 60 patients following an episode of shock or a sequence of shocks.

One hundred six (80%) of the postshock device interrogations occurred within five days of the episode of shock, while 60 occurred within one day after the shock. In particular, 46 (77%) out of 60 “first shock” episodes and 60 (82%) out of 73 subsequent episodes (P = NS) experienced by each patient were followed by an ICD interrogation within five days. A reprogramming was performed in only 68/133 (51%) episodes (43 patients). Among the first shock episodes, 37 (62%) required reprogramming, while only 31/73 (42%) episodes following the first required reprogramming (P = 0.028).

### Discussion

With regard to scheduled and unscheduled visits, CRT-ICD patients undergo device interrogation approximately every 70 days. In 35% of these device checks, no parameters are modified.

During the first six months following implant, a high number of interrogations with reprogramming are performed, ostensibly during pre-discharge sessions or early follow-up visits (e.g., wound inspection, etc.). At this point the need to optimize working parameters seems clear.

After the first six months, however, the frequency of device reprogramming declines, especially for pacing and CRT delivery parameters that are usually optimized relatively quickly after implant and maintained unmodified thereafter. On
the contrary, the number of modified “tachycardia detection” parameters seems to increase. This is due to the longer observation period considered from the six-month follow-up to the last observation (385 ± 173 days vs 182 ± 61 days). In fact these parameters are usually modified after an arrhythmia episode in order to improve the detection, thus the longer the period the higher the probability of episode occurrence.

When interpreting these results, it is important to note that the devices report the occurrence of “reprogramming” even if minor parameters are modified, or if the changes are maintained only for the duration of the interrogation session. As a consequence, the absolute number of reprogramming sessions may be overestimated. In fact, when we considered the status of 60 main parameters at the predischarge visit, the six-month follow-up, and at the last observation, we observed that only a small number of parameters are actually modified.

Specifically, the parameters for CRT delivery are the most frequently reprogrammed. In particular, pacing pulse amplitudes are adjusted in many patients during the entire follow-up. In the perspective of remote follow-up, this result could not represent a potential limitation: several algorithms of automatic threshold-capture determination have been developed and recently implemented in CRT devices.

Moreover, from predischarge to six-month visit, the atrioventricular delays are modified in a large proportion of patients: sometimes the delay optimization is performed after the predischarge visit, or during follow-up the interval programming is judged inadequate because of patient deterioration or lack of biventricular capture.

In our analysis of predictors of frequent ICD interrogations, recurrent device checks are related, as expected, to a higher incidence of shocks delivered and to lower values of mean patient activity (a measure of poor functional status). Patients with reduced activity may be those most frequently admitted to the hospital for worsening of heart failure.

A majority of postshock interrogations are performed immediately after the occurrence of an episode (less than five days). This suggests that the majority of shock episodes produces an unscheduled urgent visit for patients, many of who do not need further device adjustments. In fact, a considerable proportion of postshock interrogations does not involve reprogramming. For episodes following the first event of shock, the need to reprogram the device seems to decrease, while the urgency for care perceived by the patient seems to remain high, considering that the time from shock to interrogation remains constant.

Current guidelines suggest three to six month follow-up intervals for chronic devices. Senges-Becker et al. have recently found that routine six-month intervals appear to be safe with regard to device-related complications. Taking into consideration the ongoing rise of ICD indications and implantations worldwide, the challenge for cardiologists will be to identify effective means of handling the growing patient population, while maintaining high standards of care. Therefore, alternative approaches to frequent outpatient visits may prove useful.

Remote follow-up offers an alternative for overcrowded clinics, and considerable convenience for patients. Implantable device manufacturers are developing remote follow-up systems that provide comprehensive data that are easily transmitted by patients and viewed by physicians. However, for the sake of safety, none of these systems allow physicians to remotely reprogram the implanted device.

The most complete remote interrogation systems capture automatic device diagnostic data, stored episode electrograms, and the presenting rhythm, thus providing the clinician with information that is equivalent to that available at an office visit to assess the appropriateness of device therapies and operation. Moreover, modern ICDs automatically and continuously perform integrity and performance tests, including battery check, capacitor charge time estimation, sensed P- and R-waves measurement, lead impedance and pacing threshold assessment and adjusting, and provide detailed reports of these tests that can also be accessed remotely.

In the pre-“remote interrogation” age, Schoenfeld and Markowitz already envisaged potential scenarios deriving from the automaticity of modern devices: reduction of frequency of in-clinic follow-ups, reduction of scheduled time per appointment, and conversion of the venue from in-clinic to remote via telecommunications.

In this work we analyzed device-stored data from patients implanted with CRT-ICD, to characterize the management of implanted device patients in clinical practice in Italy, in order to figure out the potential impact of a remote follow-up system, specifically addressing the issue of the reprogramming of the ICD during follow-up.

From our results it appears that the higher number of device adjustments during the first six months of follow-up may limit the use of remote follow-up systems. However, following this initial optimization period these systems may play a more critical role.

In particular, when the ICD approaches end-of-life, remote follow-up systems may consent
closer monitoring, with reduction of ambulatory checks and increased safety.

Schoenfeld and Markowitz24 drew similar conclusions. They judged the automaticity more useful during the normal service life of the device than in the postimplant period, when there is more concern about the patient and the system.

Moreover, as Lazarus argued in a recent paper reporting the long-term application of a remote automatic monitoring system,15 in case of incidents pertaining to the long-term reliability of implanted devices, these tools may represent an attractive alternative to systematic prophylactic replacements or acceleration of ambulatory checks, providing patients with the highest level of reassurance and comfort.

Our data confirm that in the current clinical practice, the high recurrence of shock episodes causes frequent device interrogations, and thus identifies the subjects that most frequently are seeking care at the clinic, producing emergency room (ER) and unscheduled visits.

It has been noticed that with the expansion of the ICD indications to the primary prevention, the annual risk of experiencing a shock decreased significantly: in the secondary prevention AVID trial this risk was over 50% and in SCD-HeFT an annual risk of below 10% was observed.5,25 In fact in our study, where many patients were implanted for primary prevention of sudden death, we observed shock episodes only in 60 out of 217 patients over a mean follow-up of 19 months. Obviously, for the remaining patients the device interrogation consists only of a system integrity check and thus more easily it could be performed remotely.

Nonetheless, with our results we demonstrated that also a considerable portion of postshock interrogations does not involve reprogramming and therefore may be performed remotely. This can prevent many ER and clinic visits and burdensome patient travel.

The Medtronic CareLink system, which includes a patient monitor connected to a telephone line and a website where clinicians view and analyze patient device data, is currently available in the United States and to date has been adopted by more than 1,700 clinics to perform remote device checks of almost 150,000 ICD patients. During the clinical evaluation of the system,14 patients were capable of using such technology to interrogate their ICD without support from physicians, and the review of data transmissions revealed several clinically significant findings and allowed for quick clinical decisions without the need for an unscheduled office or ER visit.

In addition to the use for remote device check, these tools in conjunction with modern diagnostic features, specifically designed for the monitoring of the clinical status of the heart failure patient and the early detection of episodes of cardiac deterioration and worsening pulmonary congestion,26 could support the introduction of novel and improved management strategies of heart failure.

Limitations

This report is based on a national registry enrolling unselected patients implanted in a large number of cardiology centers well representing the current clinical practice in the country. The nonstandardized device management among centers (e.g., frequency of routine follow-up) should permit to generalize our results to other settings; nonetheless, some items should be considered.

Our results could not be applicable for devices from different manufacturers, or for institutions adopting different approaches to device follow-up and reprogramming (e.g., lack of atrioventricular delay optimization).

In this study, we considered a population of CRT-ICD patients. The severity of their disease and the complexity of the device possibly do not permit to generalize our results to all ICD patients. In fact, the observed high percentage of patients undergoing a postshock interrogation may be partially related to the need to assess the clinical status following ICD discharge. Moreover, we considered only ICD with dual chamber criteria for tachycardia detection, and this may have an impact on the rate of postshock reprogramming.

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References


Follow-up of CRT-ICD


Appendix

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