Clinical Applications of Remote Implantable Cardioverter-Defibrillator Monitoring: Current Status and Future Directions

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ABSTRACT. Implantable cardioverter-defibrillator and cardiac resynchronization devices are integral for reducing mortality in many heart failure patients. Monitoring of these devices can be facilitated using wireless remote transmission. Remote monitoring can lead to early detection of important events such as device or lead malfunction, pacing abnormalities, arrhythmias, and device-delivered antiarrhythmia therapy. Studies of remote monitoring show a reduction in the response time to clinical events. Remote monitoring may safely reduce the need for frequent office device checks and facilitate triage of device-detected events. Monitoring of several device-detected parameters can predict heart failure decompensation, and interventions based on this information may prevent heart failure hospitalization. Ongoing clinical studies will further elucidate the benefits of an expanding array of remote monitoring possibilities.

KEYWORDS. ambulatory monitoring, artificial cardiac pacing, cardiac arrhythmias, implantable defibrillators, heart failure.

Introduction

Implantable cardioverter-defibrillators (ICDs) reduce all-cause mortality by preventing sudden death in patients with a history of sustained ventricular arrhythmias and in patients with left ventricular (LV) systolic dysfunction at high risk of ventricular arrhythmias. Addition of cardiac resynchronization therapy (CRT) to ICDs (CRT-D) via biventricular pacing provides a further reduction in mortality in populations with LV systolic dysfunction, QRS prolongation and moderate-to-severe heart failure (HF) symptoms. In patients with LV systolic dysfunction, prolonged QRS and mild-to-moderate HF symptoms, CRT-D therapy reduces the incidence of HF hospitalizations, improves indices of LV function and remodeling, and may reduce mortality beyond ICD alone. In 2007, over 234,000 ICDs and over 148,000 CRT-Ds were implanted in North America. Monitoring of these devices has placed an increasing burden on the electrophysiology device community due to regularly scheduled in-office ICD follow-ups which usually do not result in clinical intervention. Expert consensus recommends ICD follow-up every 3–6 months, but clinically important events between clinic visits may be silent until the next scheduled device interrogation. Remote monitoring (RM) via periodic wireless downloading of device data can provide more frequent surveillance of devices, allowing for early problem identification and clinical intervention. RM may safely allow reduced frequency of in-office device checks, which could translate into reductions in healthcare costs.

Remote monitoring basics

RM of ICD and CRT-D devices has become an accepted and evolving strategy for device surveillance since its clinical introduction by Biotronik in 2000. Each major device manufacturer has a proprietary wireless RM
incorporation into clinical decision making. We hope algorithms for HF monitoring are being developed for better patient outcomes and health care savings. that this evolving RM armamentarium may translate into monitored (therapies with stored or real-time electrograms can be in each chamber, and review of detected arrhythmias and impedances, device-triggered alerts, sensing function, pro-

heart rhythm, modern ICD and CRT-D devices monitor a monitoring of battery voltage, magnet rate, and current available on any of these systems. Further details regarding the technical specifications of the different RM systems are reviewed elsewhere. Patterned after remote pacemaker monitoring of battery voltage, magnet rate, and current heart rhythm, modern ICD and CRT-D devices monitor a much broader array of parameters. PACing and shock lead impedance, device-triggered alerts, sensing function, programmed device parameters, percent pacing and sensing in each chamber, and review of detected arrhythmias and therapies with stored or real-time electrograms can be monitored (Table 1). Device-based parameters and algorithms for HF monitoring are being developed for incorporation into clinical decision making. We hope that this evolving RM armamentarium may translate into better patient outcomes and health care savings.

Remote monitoring of ICD and CRT-D pacemaker function

Analogous to standard pacemaker evaluation, RM can confirm proper pacing function of ICD and CRT-D devices and can identify the need for in-office reprogramming.

Table 1: Remotely monitored device parameters

<table>
<thead>
<tr>
<th>System status</th>
<th>P and R wave sensing and sensing integrity</th>
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<tr>
<td></td>
<td>Pac ing thresholds</td>
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<td></td>
<td>Lead impedance</td>
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<tr>
<td>Battery status (voltage and charge time)</td>
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<tr>
<td>Rhythm status</td>
<td>Percentage paced and sensed events</td>
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<td></td>
<td>Right ventricular pacing percentage</td>
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<td></td>
<td>Biventricular pacing percentage</td>
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<tr>
<td>Average heart rate (day and night)</td>
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<tr>
<td>Intrinsic heart rate and AV interval</td>
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<tr>
<td>Tachyarrhythmia burden</td>
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<td>Mode switch episodes</td>
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<tr>
<td>Atrial/ventricular high rate episodes</td>
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<tr>
<td>Duration/percentage of time in AT</td>
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<tr>
<td>Ventricular rate during AT</td>
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<tr>
<td>Device-delivered therapy</td>
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<td>Antitachycardia pacing</td>
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<tr>
<td>Shocks (cardioversion, defibrillation)</td>
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<tr>
<td>Device electrograms</td>
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<tr>
<td>Heart failure status (selected devices)</td>
<td></td>
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<tr>
<td>Heart rate variability</td>
<td></td>
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<tr>
<td>Patient activity level</td>
<td></td>
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<tr>
<td>Intrathoracic imped ance</td>
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Adapted from reference 12. AT, atrial tachyarrhythmia.

to optimize device function. Abnormal pacing function can contribute to worsening HF in ICD and CRT-D patients, and remote monitoring will disclose the amount of right ventricular (RV) pacing or biventricular pacing. Excessive RV pacing (above 40%) is associated with increased mortality and HF events in patients with ICDs and may predispose to ventricular arrhythmias and attenuated ICD benefit. Excessive RV pacing can often be minimized by lengthening the programmed AV delay or use of pacing-minimization device algorithms, but may require device upgrade to include CRT, particularly in patients who become pacing dependent. Inadequate percentage of biventricular pacing (below 93%) can eliminate the clinical benefits of CRT. RM can detect drops in percent biventricular pacing, warranting a full evaluation to identify the etiology. Loss of LV pacing capture in CRT-D devices due to LV lead malfunction is suggested by a dramatic change in the LV pacing resistance, which must be confirmed with formal pacing threshold testing in a device clinic. An excessively long programmed AV delay may allow intrinsic conduction through the native conduction system to pre-empt biventricular pacing, especially during exertion. Evaluation of electrograms with their marker channels will disclose ventricular sensing rather than biventricular pacing. Atrial tachyarrhythmias (ATs), supraventricular tachyarrhythmias (SVTs) or sinus tachycardia with ventricular rates exceeding the upper rate limit of the pacemaker will inhibit biventricular pacing, as can frequent ventricular premature beats. In CRT-D patients with atrial fibrillation, AV nodal ablation may be required to yield the full benefit of biventricular pacing.

Remote monitoring of ICD lead integrity

Oversensing of non-physiological signals is an important non-arrhythmic cause of inappropriate ICD shocks, generally due to lead fracture, insulation breaks, or lead–header connection problems. The majority of ICD system complications are related to lead integrity failure, which continues to be a significant clinical problem. Rates of modern ICD lead failure are relatively low (0.6%/year), but can be higher with certain high-risk ICD leads such as the Medtronic Sprint Fidelis lead (3.8%/year, hazard ratio 6.4); yearly lead failure rates appear to accelerate over time. Changes in lead impedance and short sensing intervals from lead fracture can be identified earlier with RM, allowing timely clinical intervention.

Figure 1a illustrates an abrupt increase in ICD lead pacing impedance due to a lead fracture. Electrogams and their marker channels downloaded remotely from Latitude (Figure 1b) reveal oversensing of noise and confirm the diagnosis. Changes in lead impedance alone are not adequately sensitive for lead fracture, because oversensing is often the first manifestation of lead fracture. Device reprogramming with a downloadable lead integrity algorithm may improve lead fracture detection by identifying oversensing and increases in impedance. This algorithm can prevent many inappropriate ICD shocks in patients with Sprint Fidelis leads, but remains...
unable to completely prevent inappropriate ICD shocks in patients with fractured leads. Further analysis of downloaded device data can differentiate lead fracture from connection problems and normal lead function in patients with high-impedance lead integrity algorithm alerts. Lead malfunction may also cause ventricular undersensing, which can prevent delivery of appropriate therapy for a ventricular arrhythmia. RM may detect more than 90% of lead-related complications and reduce symptomatic lead failure episodes by half, while reducing the time to recognition of lead complications. Continuous follow-up in a device clinic plus RM is recommended for patients implanted with a high-risk lead. Oversensing of physiologic signals, such as T-wave oversensing (Figure 2) or sensing of myopotentials, may be corrected with a change in device sensitivity or may require lead repositioning or implantation of a new lead.

Remote monitoring of arrhythmias

RM provides an effective means to evaluate device-detected arrhythmias and device-delivered therapy such as antitachycardia pacing (ATP), low-energy cardioversion, and defibrillation. RM systems allow accurate evaluation of stored electrograms taken during symptomatic or asymptomatic episodes of arrhythmias or device therapy. Electrogram analysis helps determine the appropriateness and effectiveness of device-delivered therapy and can identify device or lead malfunctions and
adverse effects related to device therapy. If device therapy was not effective, a change in device programming, medications, or hardware configuration may be necessary. Changes in ICD programming or antiarrhythmic medication may require formal in-hospital evaluation of cardioversion and defibrillation thresholds and ATP efficacy, such as with device-based non-invasive programmed stimulation.

**Ventricular arrhythmias and ICD shocks**

Although ICDs reduce mortality by preventing death due to ventricular arrhythmias, patients receiving ICD shock have a higher risk of both arrhythmic and pump failure death than patients without ICD shocks. Patients with more frequent ICD shocks have a higher mortality than patents with fewer ICD shocks. The mortality risk is greater for appropriate ICD shocks (treated ventricular arrhythmias) than for inappropriate ICD shocks, which are most often due to AT or other SVTs and less often due to ventricular oversensing (typically from lead failure). Inappropriate ICD shocks due to lead complications may not pose an excess mortality risk. Early detection is paramount because ICD shocks correlate with HF instability, often requiring adjustment of medications, clinical assessment and/or device reprogramming. Strategies to avoid inappropriate ICD therapy due to SVT include antiarrhythmic agents, catheter ablation, or device programming of atrial fibrillation and sinus tachycardia discriminators. ATP can be effective in more than 70% of ventricular tachycardia (VT) episodes, safely preventing unnecessary ICD shocks. Unlike ICD shocks, VT episodes terminated by ATP may not confer an adverse prognosis. ATP can occasionally be associated with proarrhythmia such as acceleration of VT
rate, in which case ATP should be eliminated. Frequent episodes of VT may require pharmacologic or ablative intervention, particularly when device therapy is ineffective. Figure 3 shows electrograms from an episode of unsuccessful ATP therapy for sustained VT, which prompted referral for VT ablation that successfully eliminated most of the patient’s ventricular arrhythmia burden.

Atrial arrhythmias

Symptomatic and asymptomatic AT are common in HF patients, and may be identified during the first post-implant year in up to one-fourth of CRT-D recipients who are in sinus rhythm at the time of implantation. Knowledge regarding the incidence, duration, frequency, and ventricular rate response of AT can be gleaned easily using RM (Figure 4). AT episodes are one of the most common clinical alerts identified by RM, and device-detected AT episodes predict worse outcomes in ICD and CRT-D patients. AT can interfere with proper device function by preventing optimal biventricular pacing or causing inappropriate ICD shocks. RM may allow earlier intervention for new or worsening device-detected AT, but it remains unclear if early detection of asymptomatic AT improves clinical outcomes. Device-detected atrial high-rate episodes correspond to AT and predict increased stroke risk. Mathematical modeling suggests that early initiation of anticoagulation based on asymptomatic device-detected AT could prevent embolism and stroke, and an ongoing randomized trial will directly test this hypothesis.

Clinical trials of remote device monitoring

Whereas transtelephonic pacemaker monitoring appears useful primarily for battery status determination, recent clinical trials using RM of ICD and CRT-D devices demonstrate earlier identification of clinical events and safe reduction in clinic visits. The CONNECT (Clinical Evaluation of Remote Notification to Reduce Time to Clinical Decision) trial randomized 1,997 Medtronic ICD and CRT-D patients to standard in-office assessment or without RM, and showed decreased time to clinical decision making by 17 days (more than 75%) and reduced healthcare utilization days with RM. The majority of remotely detected clinical events in CONNECT were prolonged AT episodes, consistent with prior studies. The TRUST (Lumos-T Safely Reduces Routine Office Device Follow-up) trial randomized 1,339 Biotronik ICD patients to standard office-only follow-up every 3 months or less frequent office visits plus RM and demonstrated a 45% reduction of in-office visits and a reduction in time to respond to clinical alerts using RM, without increasing adverse events. TRUST confirmed the safety of using RM in lieu of more frequent office visits for device checks, showing that 85% of follow-ups between 3 and 12 months after implantation can be accomplished remotely and that more than 90% of scheduled clinic device checks did not require intervention. These studies confirm the results of smaller studies suggesting that the ability of RM to reduce response time to clinical events and reduce in-hospital follow-up visits. Earlier identification of clinical events by RM did not translate into an improvement in clinical outcomes in either CONNECT or TRUST. Small studies suggest that a reduction in clinic visits by RM
may reduce healthcare costs, particularly for patients with longer driving distances, but we await formal economic analysis from larger trials for confirmation. Further cost savings are possible if early detection of clinical events by RM leads to interventions preventing hospitalization, as suggested in CONNECT by a reduced number of hospital days. The observational ALTITUDE study compared 69,556 Boston Scientific ICD and CRT-D patients who underwent RM with 116,222 similar patients who received in-office device follow-up only, and identified a 50% mortality reduction for those patients undergoing RM, with better survival at 1 and 5 years. The non-randomized design of ALTITUDE limits conclusions about causality, but baseline demographics did not differ between the two groups, so a dramatic imbalance in risk factor burden would be required to explain the survival difference. ALTITUDE is the only published study showing improved clinical outcomes associated with RM, although smaller studies suggest improvements in clinical care or patient satisfaction and quality of life without clear outcome benefits.

Remote monitoring of heart failure status

The majority of ICD and CRT-D devices are implanted in patients with HF, a group at high risk of hospitalization. Weight gain and worsening of HF symptoms may occur late and have poor sensitivity for predicting HF hospitalization. Several device-measured parameters (Table 2) can predict HF decompensation, allowing RM to facilitate early clinical intervention and potentially avert hospitalization. Intrathoracic impedance (measured between the RV lead and the device generator) varies inversely with lung fluid content, such that a decline in intrathoracic impedance suggests worsening pulmonary congestion. Intrathoracic impedance correlates inversely with pulmonary capillary wedge pressure, RV pressures, and natriuretic peptide levels. Declines in intrathoracic impedance can also occur due to device pocket complications, pneumonia, or pleural effusion. A decline in intrathoracic impedance may occur nearly 2 weeks before worsening symptoms and weight gain preceding a HF exacerbation. Declines in intrathoracic impedance may be associated with worsening atrial and ventricular arrhythmias. Intrathoracic impedance and AT demonstrate a bidirectional relationship, in which reduced intrathoracic impedance predicts more AT and increasing AT burden predicts a reduction in intrathoracic impedance. The Medtronic OptiVol feature calculates a positive numeric OptiVol index to facilitate recognition of a sustained reduction in intrathoracic impedance over time, measured in ohm-days (Figure 5a); a remote or audible alert can be sent when a preset threshold is crossed. Heart rate variability and patient activity level also decline as much as 2 weeks before HF hospitalization (Figure 5b). The Medtronic Cardiac Compass alert feature integrates the OptiVol index with patient activity, nocturnal heart rate, and heart rate variability as well as clinical events warranting provider notification such as increasing AT, reduction in biventricular pacing, or ICD shocks.
Clinical Applications of Remote Implantable Cardioverter-Defibrillator Monitoring

Table 2: Device parameters predicting heart failure decompensation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Decreased intrathoracic impedance</td>
<td>60–76%</td>
<td>90%</td>
</tr>
<tr>
<td>Elevated OptiVol index</td>
<td>76%</td>
<td>90%</td>
</tr>
<tr>
<td>Increased nocturnal heart rate</td>
<td>76%</td>
<td>90%</td>
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<tr>
<td>Decreased heart rate variability</td>
<td>76%</td>
<td>90%</td>
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<tr>
<td>Decreased patient activity level</td>
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<tr>
<td>Increased right ventricular pacing percentage</td>
<td>76%</td>
<td>90%</td>
</tr>
<tr>
<td>Increased intracardiac pressures</td>
<td>76%</td>
<td>90%</td>
</tr>
<tr>
<td>Right ventricular pressures</td>
<td>76%</td>
<td>90%</td>
</tr>
<tr>
<td>Pulmonary artery pressure</td>
<td>76%</td>
<td>90%</td>
</tr>
<tr>
<td>Left atrial pressure</td>
<td>76%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Adapted from reference 12.

Clinical studies of remote heart failure monitoring

A standard OptiVol threshold of 60 ohm-days has up to 60–76% sensitivity for detecting future HF hospitalizations in CRT-D patients,67,70,75 and many missed HF events are associated with a subthreshold decline in intrathoracic impedance. Each OptiVol threshold crossing per year predicts a 36% increased risk of HF hospitalization.67 The FAST (Fluid Accumulation Status Trial) study demonstrated that an OptiVol threshold of 60 ohm-days had superior sensitivity (76% versus 23%) and fewer false positives than daily weight monitoring for prediction of HF worsening in 156 CRT-D patients.67 The SENSE-HF study of 501 ICD and CRT-D patients showed low sensitivity (42%) and positive predictive value (38%) of the standard 60 ohm-day OptiVol threshold for predicting HF hospitalizations, especially within the first 6 months after device implantation.76 False-positive OptiVol threshold crossings occur at a rate of 0.25–1.9 events per year, including episodes in which medication titration avoided hospitalization and lesser degrees of decompensation not leading to hospitalization.67,68,76,77 The majority of OptiVol threshold crossings at 60 ohm-days may not be associated with a clinical HF event.67,68,76,77 Higher OptiVol thresholds of 100–120 ohm-days have been proposed to improve specificity,77,80 and refinements in the OptiVol algorithm may increase specificity, reduce false-positive threshold crossing events, and improve positive predictive value of OptiVol.81

Given these limitations in sensitivity and specificity, intrathoracic impedance and OptiVol cannot be used as a sole means of patient evaluation, but may supplement daily weight monitoring and standard clinical assessment to facilitate telemonitoring programs.82,83 The observational DECODE ( Decompensation Detection) study of 699 Boston Scientific CRT-D patients found that adding heart rate variability and lead (not intrathoracic) impedance monitoring to standard telemonitoring yielded poor sensitivity (<50%) for predicting HF hospitalizations, with frequent false-positive alerts (two per patient-year).84 An observational study of 532 Medtronic CRT patients showed that intrathoracic impedance monitoring using OptiVol was associated with a reduced risk of HF hospitalization.68 The observational PARTNERS-HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) study of 694 Medtronic CRT-D patients showed that the remote Cardiac Compass alert predicted a fivefold increased 1-month risk of HF hospitalization with improved sensitivity over the OptiVol index alone.77 Further research is needed to demonstrate that RM of intrathoracic impedance and other parameters can prevent HF events, and ongoing randomized studies will help to clarify this question.85

Remote hemodynamic monitoring by devices

Dedicated implantable devices can remotely monitor intracardiac hemodynamics in HF patients. Parallel to declines in intrathoracic impedance,70 intracardiac pressures rise before weight gain or symptom worsening preceding HF decompensation,86 allowing RM of hemodynamic parameters to facilitate early intervention.16 Investigational wireless implantable devices can measure pulmonary artery pressure (CardioMEMS Champion)87 or left atrial pressure (St. Jude HeartPOD),86 or estimate pulmonary capillary wedge pressure from RV hemodynamics (Medtronic Chronicle).88 Physician-directed medication titration based on device hemodynamic readings may prevent HF hospitalizations.86–88 The randomized COMPASS-HF trial of 274 advanced HF patients found that Chronicle-guided patient management produced a non-significant 21% reduction in HF events.88 HeartPOD-guided medication titration increased utilization of evidence-based HF therapies and improved functional class.86 The randomized CHAMPION trial of 550 advanced HF patients showed that Champion-guided patient management reduced total HF hospitalizations by 36%.87 Although not available on current ICD and CRT-D devices, attempts are being made to integrate intracardiac pressure monitoring into the next generation of devices.89

Integrating remote monitoring into clinical practice

A number of potential logistical and technical pitfalls limit the clinical application of RM.16 Currently available RM systems generally transmit via telephone landline only, but mobile phone compatibility is available for some models. Transmission failure can occur, but technical success rates generally exceed 90%.9 Patients must be actively involved in RM for best results, and device manufacturer representatives can often facilitate patient training and enrollment. Remote device alerts may occur in the majority of patients within 18 months after implantation,90 and frequent alerts for non-critical events may add to physician workload. Remote alert management may require individualized patient alert settings and/or a nurse-run triage system, and a specific plan for device alert management is recommended.16,62 This approach may reduce the number of alerts reaching the responsible physician by 90%, leading to a minimal increase in physician workload estimated at approximately 15 min per week per 100 patients.62,90,91
Physicians could potentially be liable if critical RM data are not acted on in a timely manner, so direct-to-physician alerts for critical events may be preferred. False-positive OptiVol alerts can occur at a rate approaching two per patient per year, but OptiVol monitoring can be successfully integrated into a multidisciplinary heart failure management strategy.
Clinical Applications of Remote Implantable Cardioverter-Defibrillator Monitoring

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Clinical Applications of Remote Implantable Cardioverter-Defibrillator Monitoring


