Telemonitoring in Patients with Congestive Heart Failure and Indication for ICD-Cardiac Resynchronization Therapy: TRIAGE-CRT

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ON BEHALF OF THE TRIAGE-CRT INVESTIGATORS

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ABSTRACT. Aims: Results from previous studies suggest that remote monitoring may benefit patients with heart failure (HF). The TRIAGE-CRT study prospectively evaluates the combined use of cardiac resynchronization therapy defibrillator (CRT-D)-based home monitoring (HM) in conjunction with weight and blood pressure (BP) electronic telemonitoring (ETM) in patients with HF. Methods and Results: 66 patients were enrolled and followed up at 3 and 6 months post implant with interim follow-up as necessary. Weight and BP were evaluated by weekly telemonitoring starting within 7–14 days post enrollment. Enrolled patients had depressed left ventricle (LV) function (age 65 ± 11 years, left ventricular ejection fraction (LVEF) 24 ± 7%, systolic resting BP 120 ± 18 mm Hg, diastolic resting BP 71 ± 15 mm Hg, etiology of HF: ischemic 58%, non-ischemic 42%). The average number of days with successful telemonitoring
triage was significantly higher for HM (135.4 ± 6.6) when compared to weight (117.7 ± 6.2) and BP (111.8 ± 6.2) ETM (p for comparison = 0.010 and 0.011, respectively). Transmission success, defined as the ratio of actual per expected daily transmission, was also higher for HM (0.806 ± 0.030) versus weight (0.683 ± 0.035) and BP (0.685 ± 0.037) (p for comparison = 0.008 and 0.011, respectively). Wireless transfer of CRT device event notifications resulted in more frequent actionable visits compared to BP or weight transmissions. Conclusions: TRIAGE-CRT demonstrates that transfer of CRT-D-based diagnostics was more frequent than weight and BP transmissions. Continuous HM in the CRT patient enables timely intervention, facilitating both remote and office-based interventions.

KEYWORDS. cardiac resynchronization therapy, heart failure, telemonitoring.

Introduction

Device-based interventions, including cardiac resynchronization therapy (CRT) and implantable cardioverter-defibrillators (ICD) are an important adjunct to traditional medical therapy for a subset of patients with heart failure (HF). In patients with systolic dysfunction and evidence of mechanical dys synchrony, cardiac resynchronization therapy significantly improves survival and quality of life.1,2 The addition of defibrillation capabilities (CRT-D) further improves symptoms and diminishes the risk of death.3–5

However, despite improved survival associated with medical and device-based therapeutics, rising costs and increasing rates of hospital readmission frame a growing need for improved longitudinal management of patients with HF.6 Among several proposed strategies, the role of remote telemonitoring remains controversial.7 In patients with systolic dysfunction, previous prospective studies and two recent meta-analyses suggest remote monitoring of weight, blood pressure (BP) and symptoms, reduces the incidence of HF hospitalization, duration of hospital stay and all-cause mortality.8–12 In contrast, a more recent randomized trial found no effect of weight and symptom-based telemonitoring on mortality or incidence of HF hospitalization.13

In addition to weight and BP, electrophysiological parameters (e.g. atrial fibrillation-burden, ventricular arrhythmias, heart rate variability) may be more sensitive indicators of clinical decompensation in HF.14 This improved sensitivity could be of particular importance to the advanced HF population, including those with CRT/CRT-D devices.

The role of electrophysiological remote monitoring in the out-patient management of patients with CRT-devices has yet to be established. TRIAGE-CRT, a single-arm, multicenter feasibility study evaluated the transmission efficacy of and correlation between CRT-device-based home Monitoring (HM) and weight and BP electronic telemonitoring (ETM) in patients with HF.

Methods

Patient population

Sixty-six patients were enrolled at 12 centers between November 2006 and January 2008. Patients selected from the investigators’ general patient population were enrolled within 45 days of CRT-D implantation (Kronos LV-T or Lumax HF-T, Biotronik, Germany). Eligible patients were adult, ambulatory, and weighed ≤400 lbs. Patients must have been able to follow and comply with the study-related procedures, including sufficient cognitive and reading skills to operate the weight and BP ETM system (Carematix Inc., Chicago, IL) and have access to a home landline telephone connection to transmit HM and ETM system information. Exclusion criteria consisted of participating in another cardiovascular clinical study and a life expectancy of <6 months. The institutional review board at each center approved the protocol, and all patients gave written informed consent.

Study procedures

At enrollment, inclusion and exclusion criteria were verified and clinical status was assessed including weight, BP, antiarrhythmic and HF medications. After enrollment, the center was required to register the subject on the HM website, order the ETM system, and educate the patient on the use of the HM and the ETM systems.

HM event notifications included HF diagnostics as well as monitoring of device integrity (Table 1). Additional notifications were activated for ventricular tachycardia (VT), ventricular fibrillation (VF), supraventricular tachycardia (SVT) and ineffective shock events. For ETM notifications, the investigator was required to activate a maximum weight and BP threshold, both of which were left to provider discretion (i.e. individualized to each patient) (recommended: 140 mm Hg; maximum number of readings: three). Measurements exceeding the indicated maximum weight and BP would be highlighted on the ETM system website for better identification and trigger an alert message via e-mail. In addition to the maximum weight alert, the ETM system activated an alert message if the patients weight increased or decreased by >2 lbs/day or >5 lbs/week (Table 1).

Within 7–14 days of HM registration and ETM system ordering, the investigational centers were required to perform weekly HM and ETM system website evaluations. Each site assigned dedicated personnel (research or device nurses) trained in both HM and ETM systems. When events from either system were flagged, the research personnel notified physician investigators or
HF nurse practitioners designated as sub-investigators. The research coordinator at each site participated in direct telephone contact with each research subject. The two website evaluations were conducted on the same day and included evaluating HM event notifications, changes in HM-parameters of clinical relevance, ETM alert messages, clinically relevant weight or BP changes, changes in event trigger settings for HM or ETM, and any actions taken (e.g. subject instructed via phone to change HF medications, antiarrhythmics, dietary plan, oxygen therapy, or if an office visit was scheduled). Additional HM/ETM website evaluations may have been performed at any time with similar documentation to the weekly HM/ETM website evaluations.

The expected days of transmission varied by the status of HM and/or ETM transmission. In patients with successful transmissions, the observation periods for weight, BP and HM started with the respective first transmission. This was done to take into account that it usually took longer for the ETM system to be ordered and installed than for automatic HM transmissions. In patients where neither system transmitted any data, the date of enrollment was taken as the start date of the observation period for all systems. If only one remote system transmitted data (e.g. HM or weight and BP data only), there was no first transmission date available for the non-transmitting system. In such cases, the first transmission date from the corresponding, successfully transmitting system was assumed as the start date of the observation period for the non-transmitting system. Each observation period ended with the date when the patient exited or completed the study.

Required office follow-ups occurred at 3 months and 6 months post implant to assess the patient’s weight, BP, and NYHA-class. In addition, the CRT-system was evaluated and changes in HF treatment, HF medications, and antiarrhythmics were recorded, as well as any adverse events. The investigational center was required to document all interim office follow-ups and hospitalizations recording the same information as required for the scheduled follow-ups. Days of data transmissions and observation periods were evaluated individually for each system (weight, BP, and HM) and patient. Days of weight and BP transmissions were retrieved from the Carematix web database server. Days of HM data transmissions were retrieved from an ORACLE database containing the HM raw data.

In patients with successful transmissions, the observation periods for weight, BP, and HM started with the respective first transmission. Each observation period ended with the date when the patient exited or completed the study at the 6-month follow-up.

### Results

#### Study population

Patient characteristics of the 66 patients included in this study are summarized in Table 2. Mean implant duration prior to enrollment was 6.1 ± 1.6 months and all patients had depressed LV function, with a mean LVEF of 24 ± 7%. The mean systolic resting BP was 120 ± 18 mm Hg and mean diastolic pressure was 71 ± 15 mm Hg. Pertinent comorbidities were present in 52 subjects, the most common being hypertension (42 subjects, 81%) and renal insufficiency (17 subjects, 33%). In total, 13 patients exited the study prior to the 6-month office follow-up (seven withdrew, one lost to follow-up, four deaths). Of the four deaths, one was non-cardiac, one was sudden cardiac, and two were secondary to decompensated HF.

#### Transmission success rates and patient compliance

The average number of successful transmissions and rates of transmission success (expressed as the ratio of actual per expected days of transmissions) are listed in Table 3. During the study period, the average number of
Of the 66 patients, four did not transmit any weight or BP data during the observation period, two patients did not transmit any HM data, and one patient did not transmit any weight, BP, or HM data.

Telemonitoring triggers initiating office follow-ups

Ninety-two (6%) of the 1,473 required telemonitoring website evaluations performed led to physician

Table 2: Patient Characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>N=66a</th>
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<tbody>
<tr>
<td>Age at enrollment (years)</td>
<td>65 ± 11</td>
</tr>
<tr>
<td>Gender: male - no. (%)</td>
<td>49 (74)</td>
</tr>
<tr>
<td>Systolic resting blood pressure (mm Hg)</td>
<td>120 ± 18</td>
</tr>
<tr>
<td>Diastolic resting blood pressure (mm Hg)</td>
<td>71 ± 15</td>
</tr>
<tr>
<td>Cardiovascular status</td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>24 ± 7</td>
</tr>
<tr>
<td>Etiology of heart failure at enrollment – no. (%) N=65</td>
<td></td>
</tr>
<tr>
<td>Ischemic</td>
<td>38 (58)</td>
</tr>
<tr>
<td>Pertinent comorbidities at enrollment – no. (%) N=52</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>42 (81)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>17 (33)</td>
</tr>
<tr>
<td>Pulmonary edema</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>19 (37)</td>
</tr>
<tr>
<td>ICD-indications at enrollment – no. (%)</td>
<td></td>
</tr>
<tr>
<td>Prophylactic indication</td>
<td>56 (85)</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>11 (17)</td>
</tr>
<tr>
<td>Syncope with documented ventricular tachycardia and LVEF &lt; 40%</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Non-sustained VT post MI and LVEF &lt; 40%</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Survived cardiac arrest and inducible VT/VF</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Heart failure class – no. (%)b</td>
<td></td>
</tr>
<tr>
<td>I – 2 (3%)</td>
<td></td>
</tr>
<tr>
<td>II – 20 (30.8%)</td>
<td></td>
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<tr>
<td>III – 43 (66.2%)</td>
<td></td>
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<tr>
<td>IV – 0 (0%)</td>
<td></td>
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</table>

aNumber of patients for each category, unless otherwise specified.
bPresence of Class I and II HF is reflective of the enrollment criteria, which allowed for enrollment up to 45 days following device placement, at which time functional benefit may have accrued.

LVEF, left ventricular ejection fraction; VF, ventricular fibrillation; VT, ventricular tachycardia.
intervention in the form of: medication change (n=26; 28%), scheduling urgent office visits (n=19; 21%), dietary plan change (n=3; 3%), or other actions (e.g. device reprogramming) (n=44; 48%). Seventeen unscheduled office visits in 12 patients were initiated by HM event notifications, independent from office visits scheduled following required telemonitoring evaluations. There were no unscheduled office visits initiated by alerts from weight and BP telemonitoring. The most common trigger for an unscheduled, HM-triggered office visit was ‘low percentage of CRT pacing’ (n=6; 35%). Other reasons included VT/VF/AF episodes (n=4; 24%) and high PVC counts (n=1; 6%). In four cases, no particular HM event notification was specified. Actions taken at the unscheduled HM-initiated office visits included device reprogramming (n=8; 47%), medication changes (n=7; 41%) and hospital admission (n=2; 12%).

Compliance

All sites in the protocol were required to perform weekly HM and ETM evaluations, in addition to scheduled 3- and 6-month follow-up evaluations. Of the total 1,577 required follow-ups, there was a compliance rate of 96% (1,509/1,577) during the course of the study.

Discussion

The TRIAGE-CRT feasibility study assessed the role of traditional weight and BP telemonitoring in combination with device-based HM in patients with CRT-D devices. This is the first report directly comparing the efficacy of traditional monitoring parameters (weight, BP) to device-based monitoring in the CRT population. Our results demonstrate significantly higher rates of transmission of HM parameters (normalized transmission success: 80.6%) when compared to transmission of weight and BP telemonitoring data (normalized transmission success: 68.3% and 68.5%, respectively). HM parameters were also more likely to trigger an office visit than telemonitoring parameters.

The effectiveness of a remote monitoring intervention depends on several important factors; namely, the population selected for monitoring, the monitoring parameter used as a proxy for clinical decompensation, the intensity of monitoring (continuous versus intermittent), patient compliance with the monitoring intervention, adequate physician or caregiver review of monitoring data, and effective communication of potential therapeutic changes between patient and provider.7 Previously successful telemonitoring strategies in patients with HF used traditional weight and symptom-based algorithms in patients with evidence of systolic dysfunction and Class II–IV symptoms (e.g. WHARF, SPAN-CHF, TEN-HMS).8–11 These telemonitoring studies required a significant nurse/physician monitoring infrastructure. Rates of patient compliance ranged from 88% to 90% at 6 months (WHARF, TEN-HMS), to 63% at 14 months (TEN-HMS). In contrast, the recent Tele-HF trial, which also used weight and symptom-based monitoring, found no reduction in mortality or HF hospitalization at 6 months.12 Sub-group analysis did not find any marginal benefit for patients stratified by systolic function or HF class. In this latter study, patient adherence to the telemonitoring intervention was 55% at 6 months. Consistent with previous studies, we found rates of transmission for weight and BP data of approximately 68% at 6 months. The transmission rate (81%) of HM parameters in our study was significantly higher than weight/BP transmission and similar in magnitude to compliance rates of previously successful telemonitoring interventions.

In addition to patient compliance, another critical determinant of telemonitoring efficacy is the sensitivity of the monitoring parameters used as a proxy for clinical decompensation. Traditional telemonitoring strategies have used weight and symptom-based triggers.11 More recent invasive hemodynamic data, however, suggest that perturbations of weight may not correlate with the physiologically relevant changes in intra-cardiac pressures that typically precede clinical decompensation.14 In contrast to weight-based changes, electrophysiological perturbations in patients with CRT devices (e.g. transthoracic impedance, physical activity log, heart rate variability) may precede clinical symptoms by several days, better identifying patients at risk for decompensation.15 By example, in the recent PARTNERS-HF study, the addition of CRT-based triggers to a model including age, medications, gender, and diabetic status, improved prognostic accuracy in predicting HF hospitalization.16 In addition, device-specific triggers (e.g. percentage of CRT pacing) may be particularly useful in preventing decompensation in the subset of patients with HF undergoing CRT.

In our cohort, all HM-associated office visits were associated with actionable changes in management. It is nevertheless important to note that any potential benefit from earlier detection of decompensation may be counterbalanced by the risk of overly sensitive triggers and unnecessary office visits. Finally, telemonitoring efficacy is also related to the ease of telemonitoring data review. Our finding of 96% physician compliance with the monitoring intervention suggests that the HM system is a practical and usable telemonitoring tool. Of note, given the method of enrollment, the degree of compliance may have been influenced by selection bias.

TRIAGE-CRT shows that device-related transmission of electrophysiological data is feasible and more successful than transmission of traditional monitoring parameters in patients with HF and CRT-D devices. The recently published TRUST study in patients with ICDs showed similar feasibility and superiority of monitoring when compared to conventional office follow-up.17 Indeed, although retrospective analysis of the ALTITUDE cohort suggests a possible survival benefit for remote monitoring in patients with CRT devices,18 prospective data are lacking. Hemodynamic monitoring using device-based sensor strategies, coupled with the HM described here, could serve as a better indicator of clinical decline when compared to traditional markers such as weight and BP.
As a feasibility study, these data cannot establish whether the superior transmission of electrophysiological parameters reduces the incidence of HF decompensation and/or mortality.

**Limitations**

The small size of our study limited our ability to perform relevant comparative analyses with an ETM-only control group. As TRIAGE-CRT was a feasibility study, it was under-powered to generate meaningful comparisons with historical controls for clinical end-points including HF-hospitalizations and mortality. In addition, as discussed above, HM triggers may precipitate unnecessary office visits. The relative economic burden of unnecessary visits, balanced against the potential benefit of reduced HF hospitalizations, remains an open question in HF telemonitoring for patients with CRT-D devices.

**Conclusion**

In conclusion, TRIAGE-CRT demonstrates that transmission of CRT-D based diagnostics was more frequent than weight and BP transmissions. Device-based diagnostics have a higher propensity to initiate an office visit when compared to BP and weight transmission. Automated HM in the CRT patient enables timely intervention, facilitating both remote and office-based interventions. Future prospective studies are needed to establish the potential clinical and economic benefits of telemonitoring in patients with advanced HF and CRT-D devices.

**References**