Impact of Cardiac Resynchronization Therapy on Hospitalizations in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial

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Background—This study reports the impact of cardiac resynchronization therapy (CRT) on hospitalizations in patients randomized to implantable cardioverter-defibrillator (ICD) or ICD-CRT in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT).

Methods and Results—Hospitalization rates and lengths of hospital stay were compared between the 2 groups. At the 18-month follow-up, the numbers of patients hospitalized for any cause were similar in the ICD (n=351, 38.8%) and ICD-CRT (n=331, 30.0%) groups. The number of patients hospitalized for heart failure was significantly lower in the ICD-CRT (n=101, 11.3%) compared with the ICD (n=141, 15.6%; P=0.003) group. The number of patients hospitalized for a device-related indication was similar in the ICD-CRT group (n=147, 16.4%) and ICD group (n=126, 13.9%; P=0.148). The total number of hospitalizations for any cause (n=1448 versus n=1553; P=0.042), any cardiovascular cause (n=667 versus n=790; P=0.017), and any heart failure cause (n=385 versus n=505; P<0.0001) was significantly lower in ICD-CRT group compared with the ICD group, whereas the number of hospitalizations for device-related causes was significantly higher in the ICD-CRT group compared with the ICD group (246 versus 159; P<0.001). Although the reduction in hospitalizations for heart failure in the CRT-ICD group was offset by an increased number of hospitalizations for device-related indications, the length of hospital stay for any cause was significantly shorter in the ICD-CRT group (8.83±13.30 days) compared with the ICD group (9.59±14.40 days; P=0.005).

Conclusion—ICD-CRT therapy significantly reduces hospitalizations and total days in hospital in patients with New York Heart Association class II/III heart failure compared with ICD therapy despite increased admissions for device-related indications.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00251251.

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Key Words: cardiac resynchronization therapy ■ heart failure ■ hospitalization

Cardiac resynchronization therapy (CRT) has evolved as an important device therapy in the management of patients with symptomatic heart failure (HF) despite optimal medical therapy.1-8 Recently, CRT therapy has been shown to reduce hospitalizations for HF in patients with mild to moderate HF.4-8 The Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT) reported that patients with mild to moderate HF and depressed left ventricular systolic function in association with an intraventricular conduction delay randomized to an implantable cardioverter-defibrillator (ICD) plus CRT experienced improved survival and were significantly less likely to be hospitalized for HF compared with the group randomized to ICD therapy alone.4 This prespecified study within RAFT presents a detailed analysis of the causes of hospitalization, hospitalization rates, and hospitalization lengths of stay in the RAFT cohort.

Clinical Perspective on p 2030

Methods

The study design9 and results of RAFT8 have previously been published. Patients were enrolled at 24 centers in Canada, 8 centers in...
Europe and Turkey, and 2 centers in Australia. Enrollment criteria included New York Heart Association (NYHA) class II or III HF symptoms on optimal medical therapy, a left ventricular ejection fraction ≤30%, an intrinsic QRS duration ≥120 milliseconds or a paced QRS duration ≥200 milliseconds, and a primary or secondary prevention indication for ICD therapy for the prevention of sudden cardiac death. The protocol was revised in February 2006 to include patients with NYHA class II symptoms only after the publication of the Cardiac Resynchronization–Heart Failure Trial. Patients were excluded from participation if they had a major coexisting illness or a recent cardiovascular event. All patients gave written informed consent to participate.

Eligible patients were randomly assigned in a 1:1 ratio to receive an ICD or an ICD with CRT stratified according to clinical center, the underlying atrial rhythm, and intention to implant a single- or dual-chamber ICD. Patients were seen in follow-up 1 month after device implantation and then every 6 months for at least 18 months until the end of the trial. The patients and their general healthcare providers, including the healthcare team responsible for HF management and reporting of clinical events, were blinded to treatment assignments.

At baseline, all patients underwent a medical history and physical examination, a 12-lead ECG, a 6-minute walk test, a quality-of-life assessment, and documentation of optimal medical therapy with a β-blocker, an angiotensin-converting enzyme inhibitor or angiotensin-receptor blocker, spironolactone, aspirin, and statins when appropriate.

Outcome Measures

All deaths and hospitalizations were adjudicated by an event committee whose members were blinded to study group assignments. This adjudication was based on review of the submitted case report forms and accompanying information, including the emergency department record, admission and progress notes, consultation notes, discharge summary, chest x-ray reports, and other diagnostic test results. A third reviewer was assigned if there was not consensus of the cause of hospitalization between the initial 2 adjudicators.

The index hospitalization for initial device implantation was not included in this analysis unless associated with a significant complication that prolonged the hospital stay. Hospitalizations were classified as cardiovascular or noncardiovascular. Cardiovascular hospitalizations were further categorized as HF, myocardial ischemia, arrhythmia (with further subgrouping based on type), thromboembolic events, cerebrovascular, device or procedure related, and other cardiovascular causes, including cardiac transplantation. Hospitalization for HF was defined as admission to an institution for ≥24 hours with a diagnosis of and subsequent treatment for HF. If HF developed during an admission for another medical problem, this was not classified as an HF hospitalization. The criteria for an HF admission included documentation of the signs and symptoms of HF, including dyspnea, progressive peripheral edema, elevated jugular venous pressure, pulmonary edema, chest x-ray findings of interstitial edema, and the need for intravenous diuretics, as well as vasodilators or inotropic agents.

Noncardiovascular hospitalizations were further categorized as pneumonia, chronic obstructive lung disease, hypotension, renal failure, cancer, diabetes mellitus, gastrointestinal, peripheral vascular disease, and other medical causes. Hypotension was defined as symptoms attributed to documented low blood pressure in the absence of any other cause. Other causes included the aggregate of admissions for other medical reasons such as anemia, infection, sepsis, atypical chest pain, and surgical indications such as joint replacement or cholecystectomy.

All adverse events occurring within 30 days after ICD implantation were adjudicated as related or unrelated to the ICD. Device procedure-related events were further categorized as infection, pocket seroma/hematoma, lead dislodgement, lead replacement, pulse generator replacement, and inappropriate shocks. Infection was defined as findings of systemic infection or findings of a pocket infection, including purulent drainage or positive cultures requiring system explantation and antibiotic therapy. Pocket seroma/hematoma was defined as significant swelling of the pocket requiring either surgical intervention or medical observation. Lead dislodgement was defined as evidence of lead dislodgement requiring repositioning. Lead replacement was defined as lead failure caused by dislodgement, diaphragmatic stimulation, high pacing thresholds, or sensing/detection malfunctioning requiring lead replacement. Pulse generator replacement was documented for expected end-of-life battery depletion, premature battery failure, pulse generator failure, pulse generator replacement because of a health safety advisory on the device, or other causes. Inappropriate shocks were documented for oversensing, sinus tachycardia, or atrial tachyarrhythmia.

Statistical Analysis

All analyses were performed according to the intention-to-treat principle. Continuous data are presented as means±SD. Differences in baseline demographic variables and hospitalization frequency were compared by 2-sample t tests for continuous variables and the χ² test or Fisher exact test for categorical variables. Patients in RAFT were followed up for a variable amount of time because of either the timing of their enrollment in the study or death. The RAFT investigators reported improved survival in the group randomized to ICD-CRT compared with ICD; thus, the follow-up duration of survivors was longer. Furthermore, some patients had multiple admissions for HF over time; therefore, to provide a more accurate estimate of the difference between treatment groups, counts of events (number of hospitalizations and days in hospital) per 100 patient-years at risk (PYR) were calculated. Differences in the number of hospitalizations were evaluated by use of a negative binomial model with an offset variable to account for the variable time in the study. Differences in hospitalization length of stay were evaluated by use of a linear mixed model using the log of hospital days for the outcome and a random effect for person. In addition, for analyzing time to multiple events (ie, hospitalizations and death), marginal and multistate models for the joint analysis of survival and time to HF hospitalizations were considered. In particular, the multistate model incorporates important features in the analysis of HF hospitalizations and death such as multiple ordered events per subject, event history data, accommodation of competing risks, and the distinction between 2 different clinical events: death and hospitalization. The R software with mstate package was used for this analysis.

A comparison of hospitalization days was also undertaken to determine whether there were significant differences between geographic regions. Differences in survival free from hospitalization for HF are shown by Kaplan-Meier analysis with comparisons using the log-rank test.

Results

Study Population

The characteristics of the RAFT study population have been previously reported. The majority were male (83%) with a mean age of 66±9 years. The majority had ischemic heart disease (66%) with a mean left ventricular ejection fraction of 23±5% and NYHA functional class II symptoms (80%). The clinical characteristics of the 2 groups were similar. As a result of the increased mortality in the ICD group, the follow-up duration was shorter (39.2±19.4 months) compared with the ICD-CRT group (41.2±19.6 months; P=0.031).

Number of Patients Hospitalized

The proportion of patients hospitalized within 18 months of randomization according to treatment assignment is shown in Figure 1. The proportion of patients hospitalized within this time frame for any cause was similar in the ICD (n=351, 38.8%) and ICD-CRT (n=331, 37.0%) groups (P=0.437). In contrast, the proportion of patients hospitalized for cardiovascular...
causes was lower in the ICD-CRT group (n=166, 18.6%) compared with the ICD group (n=215, 23.8%; difference, 49 patients; absolute reduction, 5.2%; P=0.008). The proportion of patients hospitalized for HF was also significantly lower in the ICD-CRT group (n=101, 11.3%) compared with the ICD group (n=141, 15.6%; P=0.009; difference, 40 patients; absolute reduction, 4.3%). Over this time frame, slightly more patients in the ICD-CRT group were likely to be hospitalized for device-related events (n=147, 16.4%) compared with the ICD group (n=126, 13.9%; P=0.148; difference, 21 patients; absolute increase, 2.5%), but this difference was not statistically significant.

**Total Number of Hospitalizations and Total Days Hospitalized**

The total number of hospitalizations and the proportion of hospitalizations for specific indications and total hospitalizations per 100 PYR over the entire course of the study are shown in Table 1. The total number of hospitalizations was lower in the ICD-CRT group (n=1448) compared with the ICD group (n=1553; difference, 105 hospitalizations; P=0.042). The total number and proportion of these hospitalizations that were for cardiovascular causes were significantly lower in the ICD-CRT group (n=667, 46.1%) compared with the ICD group (n=790, 50.9%; difference, 123 hospitalizations; absolute reduction, 4.8%; P=0.017). The reduction in hospitalization for cardiovascular causes was due predominantly to the reduction in hospitalizations for HF, which was also significantly lower in the ICD-CRT group (n=385, 26.6%) compared with the ICD group (n=505, 32.5%; P<0.0001; difference, 120 hospitalizations; absolute reduction, 5.9%). In contrast, the number and proportion of hospitalizations for device-related events were significantly higher in the ICD-CRT group (n=246, 17.0%) compared with the ICD group (n=159, 10.2%; P<0.001; difference, 87 hospitalizations; absolute increase, 6.8%).

The total number of hospitalizations for HF when normalized per 100 PYR was lower in the ICD-CRT group (12.5 per 100 PYR) compared with the ICD group (17.1 per 100 PYR; difference, 4.6 per 100 PYR), and the total number of hospitalizations for device-related events per 100 PYR was higher in the ICD-CRT group (8.0 hospitalizations per 100 PYR) compared with the ICD group (5.4 hospitalizations per 100 PYR; difference, 2.6 per 100 PYR; Table 1).

The higher number of device-related hospitalizations in the ICD-CRT group was offset by the lower number of hospitalizations for HF, resulting in the finding that the total number of hospitalizations for HF or device-related causes was not significantly different in the ICD-CRT group (631, 43.6%) compared with the ICD group (664, 42.8%; difference, 33 hospitalizations; P=0.101).

The total number of days hospitalized, mean duration of hospitalization per hospital stay, and total days hospitalized per 100 PYR are shown in Table 2. The length of hospital stay (per admission) for any reason was significantly shorter in the ICD-CRT group compared with the ICD group (P=0.005). The difference in days hospitalized was 2113 days or 88 days per 100 PYR. The length of hospital stay for any cardiovascular cause, HF cause, or device-related cause was similar for both groups. The length of hospital stay for either HF or a device-related cause was significantly shorter in the ICD-CRT group compared with the ICD group (P=0.022). The average duration of hospitalization for device-related causes was 6.3±9.1 days compared with 11.3±13.6 days for an HF admission. The difference in total days hospitalized for either HF or a device-related cause between the ICD-CRT and ICD groups was 1134 days or 46 days per 100 PYR.

The length of hospital stay by NYHA functional class for all cause, cardiovascular cause, HF, or device-related cause is shown in Table 3. The length of hospital stay was significantly shorter for all cause (P=0.018) and cardiovascular cause (P=0.003) in the NYHA class II subgroup compared with the NYHA class III subgroup. The length of hospital stay was significantly shorter for all cause in the NYHA class II (P=0.036) and III (P=0.043) ICD-CRT subgroups compared with the ICD subgroups. The length of stay for either HF or a device-related cause was significantly shorter in the NYHA class III ICD-CRT subgroup compared with the NYHA class III ICD subgroup (P=0.006).

**Effect of CRT on Recurrent HF Hospitalization and Death**

We have previously reported that ICD-CRT significantly reduced the combined end point of death or hospitalization for HF compared with ICD and that survival was significantly improved with ICD-CRT. The effect of CRT on recurrent hospitalization for HF and death assessed with a multistate model is shown in Figure 2. Patients in the ICD-CRT group had a significantly lower risk for first HF hospitalization (hazard ratio=0.67; 95% confidence interval, 0.55–0.81; P<0.0001). In addition, patients in the ICD-CRT group experienced a
lower risk of death after the first HF hospitalization (hazard ratio=0.53; 95% confidence interval, 0.31–0.91; \(P=0.022\)). Figure 3 shows the time to first HF hospitalization, which was significantly longer in the ICD-CRT group compared with the ICD group (\(P<0.001\)). Lack of CRT therapy (odds ratio=1.30; 95% confidence interval, 1.12–1.53) was an independent predictor of hospitalization for HF.

### Hospitalizations for HF by Geographic Region

Table 4 shows the number of hospitalizations for HF and average length of stay per HF admission by geographic region, including 4 geographic regions within Canada. There were no significant differences in the number of days hospitalized for HF by geographic region.

### Device-Related Hospitalizations

The total number of hospitalizations and total number of days hospitalized for device-related events by subgroup are shown in Table 5. Lead repositioning, lead failure, a reattempt to implant a left ventricular pacing lead, and ICD pulse generator replacement for expected battery depletion were the major causes of the increased rate of hospitalization in the ICD-CRT group. More patients in the ICD group were hospitalized for inappropriate shocks compared with the ICD-CRT group. The number of cases resulting from pocket seroma/hematoma requiring surgical intervention or pocket infection/ICD system infection requiring medical intervention was slightly higher in the ICD-CRT group. During the study, 103 patients (11.4%) were upgraded to ICD-CRT therapy. Failure of the Sprint Fidelis lead models, which were recalled during the course of this clinical trial, accounted for 45 device-related hospitalizations (11.1%) and 293 total days hospitalized (11.5%) for device-related causes.

### Discussion

RAFT demonstrated that ICD-CRT significantly reduced the risk of death or hospitalization for HF in patients with NYHA.
### Table 2. Length of Hospital Stay (per Stay)

<table>
<thead>
<tr>
<th></th>
<th>ICD (n=904)</th>
<th>ICD – CRT (n=894)</th>
<th>Linear Mixed Model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Days Hospitalized</td>
<td>Mean±SD</td>
<td>Days per 100 PYR</td>
</tr>
<tr>
<td>All-cause hospitalization</td>
<td>14896</td>
<td>9.59±14.40</td>
<td>504.44</td>
</tr>
<tr>
<td>Medical hospitalizations</td>
<td>13771</td>
<td>9.86±14.69</td>
<td>466.34</td>
</tr>
<tr>
<td>CV hospitalization</td>
<td>7900</td>
<td>10.00±12.75</td>
<td>267.52</td>
</tr>
<tr>
<td>HF hospitalization</td>
<td>5721</td>
<td>11.3±13.63</td>
<td>193.74</td>
</tr>
<tr>
<td>Ischemic hospitalization</td>
<td>651</td>
<td>6.85±7.88</td>
<td>22.05</td>
</tr>
<tr>
<td>Arrhythmic hospitalization</td>
<td>1090</td>
<td>7.32±11.46</td>
<td>36.91</td>
</tr>
<tr>
<td>Bradyarrhythmia</td>
<td>12</td>
<td>6.00±4.24</td>
<td>0.41</td>
</tr>
<tr>
<td>Atrial tachyarrhythmia</td>
<td>203</td>
<td>5.97±5.15</td>
<td>6.87</td>
</tr>
<tr>
<td>Ventricular tachyarrhythmia</td>
<td>875</td>
<td>7.74±12.84</td>
<td>29.63</td>
</tr>
<tr>
<td>Thromboembolic hospitalization</td>
<td>414</td>
<td>11.19±13.27</td>
<td>14.02</td>
</tr>
<tr>
<td>Stroke or TIA</td>
<td>367</td>
<td>11.47±13.91</td>
<td>12.43</td>
</tr>
<tr>
<td>Other CV hospitalization</td>
<td>24</td>
<td>6.00±3.27</td>
<td>0.81</td>
</tr>
<tr>
<td>Implant- or device-related hospitalization</td>
<td>1125</td>
<td>7.08±11.21</td>
<td>38.10</td>
</tr>
<tr>
<td>30-d postimplantation related</td>
<td>167</td>
<td>8.79±12.34</td>
<td>5.66</td>
</tr>
<tr>
<td>90-d postimplantation related</td>
<td>254</td>
<td>7.26±9.54</td>
<td>8.60</td>
</tr>
<tr>
<td>Total HF and implant/device-related hospitalization</td>
<td>6846</td>
<td>10.31±13.21</td>
<td>231.83</td>
</tr>
<tr>
<td>Total non-CV hospitalization</td>
<td>5871</td>
<td>9.72±16.90</td>
<td>198.81</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>503</td>
<td>8.67±7.20</td>
<td>17.03</td>
</tr>
<tr>
<td>COPD</td>
<td>150</td>
<td>6.82±10.66</td>
<td>5.08</td>
</tr>
<tr>
<td>Hypotension</td>
<td>62</td>
<td>3.65±3.20</td>
<td>2.10</td>
</tr>
<tr>
<td>Renal failure</td>
<td>455</td>
<td>10.83±15.86</td>
<td>15.41</td>
</tr>
<tr>
<td>Cancer</td>
<td>350</td>
<td>9.21±8.16</td>
<td>11.85</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>121</td>
<td>8.64±10.02</td>
<td>4.10</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>484</td>
<td>7.01±7.42</td>
<td>16.39</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>337</td>
<td>16.39±17.72</td>
<td>11.41</td>
</tr>
<tr>
<td>Other medical hospitalization</td>
<td>3409</td>
<td>10.50±20.87</td>
<td>115.44</td>
</tr>
</tbody>
</table>

CRT indicates cardiac resynchronization therapy; CV, cardiovascular; COPD, chronic obstructive pulmonary disease; HF, heart failure; ICD, implantable cardioverter-defibrillator; PYR, patient-year at risk; and TIA, transient ischemic attack.
class II or III HF; left ventricular systolic dysfunction, and a wide QRS. The present study extends the observations of RAFT by providing detailed information on hospitalizations and length of stay. The major findings of this study are the following: (1) ICD-CRT therapy reduced the number of hospitalizations for all cause, cardiovascular cause, or HF in the RAFT population with NYHA class II/III HF symptoms but increased the total number of hospitalizations for device-related events; (2) ICD-CRT therapy significantly reduced the length of hospital stay for any cause and for the combined end point of hospitalization for HF or device-related cause; and (3) the benefit of CRT on reducing hospital length of stay was observed in both patients with NYHA class II and those with class III symptoms.

**CRT and Hospitalizations for HF**

The Comparison of Medical Therapy, Pacing and Defibrillator in Heart Failure (COMPANION) investigators reported that CRT reduced hospitalizations and hospitalization days normalized per patient year of follow-up for all cause, cardiovascular cause, and HF cause. However, hospitalizations for initial implantation of the device or elective implantation of a device were not included in that data analysis. The COMPANION investigators did not report the hospitalization data for device-related causes. The Cardiac Resynchronization in Heart Failure (CARE-HF) investigators reported that the overall number of days spent in hospital was similar in patients randomized to CRT (20.7 days) and the medical therapy group (22.4 days). Patients randomized to CRT spent more days in hospital within 3 months of randomization compared with the medical group as a result of device implantation. Thereafter, the CRT group spent fewer days in hospital owing to a reduction in cardiovascular events, including a reduced hospitalization for worsening HF compared with medical therapy alone (hazard ratio, 0.54; 95% confidence interval, 0.43–0.68). However, the details of hospital length of stay for HF have not been published.

The present study is the first to present detailed data on hospitalization and length of stay in patients randomized to ICD or ICD-CRT. In the Multicenter Automatic Defibrillator Implantation Trial With Cardiac Resynchronization Therapy (MADIT-CRT), CRT was associated with a significant reduction in the risk of a first HF event and a similar reduction in subsequent HF events. This analysis was based on a full efficacy analysis and included patients who crossed over to CRT after an initial HF event. However, on the basis of the intention-to-treat analysis, CRT was not associated with a statistically significant reduction in subsequent HF events. Several important differences between MADIT-CRT and RAFT must be emphasized. In MADIT-CRT, an HF event was defined as signs and symptoms of congestive HF responsive to intravenous therapy on an outpatient visit or augmented HF therapy with oral or parenteral medications during hospitalization. In RAFT, however, HF events were classified as admission to a healthcare facility for >24 hours for treatment of symptomatic HF. Twenty percent of patients in RAFT had NYHA class III symptoms, whereas these patients were excluded from MADIT-CRT. Patients in RAFT were followed up for a longer period (40 months), and there were fewer crossovers to CRT after the first HF episode in RAFT, thus allowing a more robust assessment of the impact of CRT on HF outcomes over time.

In the present study, the reduction in the number of patients hospitalized for HF was offset by the increased number of patients hospitalized for device-related complications associated with CRT. However, hospitalization for device-related causes was shorter than hospitalization for HF. Furthermore,
some patients had multiple admissions for HF over time. In RAFT, survival was improved in patients randomized to ICD-CRT. Thus, presenting the data on the total number of hospitalizations and total days in hospital per 100 PYR provides a more accurate estimate of the benefit of CRT because the treatment effect of CRT on hospitalizations would be attenuated by the competing risk of death resulting from cardiovascular causes or other comorbidities. Furthermore, using a multistate model to examine the effect of CRT on recurrent hospitalizations for HF and death, we have demonstrated that CRT lowered the risk for first HF hospitalization, and improved survival in the ICD-CRT group was observed after the first HF hospitalization.

The benefit of CRT for reducing the number of hospitalizations and hospital length of stay in RAFT was observed in patients with NYHA class II and III symptoms. Readmission to hospital for recurrent HF therapy is not infrequent and is costly. The reduction in hospitalizations and hospitalization days with CRT therapy observed in RAFT would be anticipated to result in substantial healthcare savings, but the magnitude of this benefit awaits the completion of a detailed cost-effectiveness analysis.

Given that hospital stay may vary dramatically by geographic region, we examined the duration of hospital stay for HF by geographic region: Australia, Canada, Europe, and Turkey. The average length of stay was similar between regions. In addition, there were no significant differences in average length of stay between geographic regions within Canada. The average duration for an HF hospitalization in the RAFT population is similar to what has been reported by other investigators in other geographic regions, including Canada, Italy, New Zealand, and Spain. Shorter lengths of stay have been reported in the United States by the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF) investigators. The average length of stay reported for Medicare and Medicaid patients with systolic HF is also shorter (7 days) compared with the RAFT population. Because patients who might be considered candidates for CRT are likely sicker, it is possible that hospital length of stay for HF might be longer in this cohort. Variations in length of stay may be influenced by medical resource limitations in a capitated system (wait times for diagnostics tests or procedures), as well as outpatient follow-up resources. We believe that the findings in this study apply...
to patients in the United States, although the magnitude of benefit might differ.

**Device-Related Hospitalizations**

Although CRT reduced HF hospitalizations in RAFT, there was a corresponding increase in the number of hospitalizations for device-related causes related primarily to lead repositioning or lead replacement and replacement of the pulse generator as a result of battery depletion. In current practice, device-related complications are expected to be less. Some of the lead failures were Sprint Fidelis leads, which are known to have an increased risk of failure and were subjected to a health safety advisory during the course of the trial. In addition, advances in device technology have improved the battery longevity of ICDs; hence, device replacement rates are expected to decline over time. Furthermore, as indications for CRT have expanded and implantation experience and volumes have increased at individual centers, complications related to the implantation procedure are predicted to decline. Our preliminary data suggest a temporal improvement in some device-related events.

**Potential Limitations**

In the RAFT population, follow-up was longer in the ICD-CRT group because of improved survival. This follow-up difference may have contributed to bias in the data analysis, although the ICD-CRT group experienced fewer hospitalizations and days in hospital despite the longer follow-up period. Because many patients experienced multiple hospitalizations and the average length of stay was not normally distributed, specific statistical models were used to address these issues. Normalizing data per patient time assumes that event rates are constant, which may not be the case. The time to first hospitalization for HF event analysis addresses this concern and demonstrates the impact of CRT therapy on reducing HF hospitalizations. Furthermore, the competing risk analysis addresses this limitation in part.

**Table 5. Device-Related Hospitalizations**

<table>
<thead>
<tr>
<th>Event</th>
<th>ICD</th>
<th>Events per 100 PYR</th>
<th>Days Hospitalized</th>
<th>ICD - CRT</th>
<th>Events per 100 PYR</th>
<th>Days Hospitalized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead reposition</td>
<td>15</td>
<td>0.51</td>
<td>38</td>
<td>1.24</td>
<td>46</td>
<td>3.07±2.66</td>
</tr>
<tr>
<td>Lead failure (with replacement)</td>
<td>14</td>
<td>0.47</td>
<td>34</td>
<td>1.11</td>
<td>76</td>
<td>5.43±2.82</td>
</tr>
<tr>
<td>Reattempt to implant LV lead</td>
<td>2</td>
<td>0.07</td>
<td>18</td>
<td>0.59</td>
<td>7</td>
<td>3.50±0.71</td>
</tr>
<tr>
<td>Cardiac perforation</td>
<td>1</td>
<td>0.03</td>
<td>1</td>
<td>0.03</td>
<td>13</td>
<td>NA</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>1</td>
<td>0.03</td>
<td>1</td>
<td>0.03</td>
<td>13</td>
<td>NA</td>
</tr>
<tr>
<td>Expected end of battery life</td>
<td>7</td>
<td>0.24</td>
<td>64</td>
<td>2.08</td>
<td>37</td>
<td>5.29±5.25</td>
</tr>
<tr>
<td>Premature battery depletion</td>
<td>3</td>
<td>0.10</td>
<td>5</td>
<td>0.16</td>
<td>4</td>
<td>1.33±0.58</td>
</tr>
<tr>
<td>Reimplantation of entire system</td>
<td>1</td>
<td>0.03</td>
<td>5</td>
<td>0.16</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>Inappropriate shocks</td>
<td>30</td>
<td>1.01</td>
<td>20</td>
<td>0.65</td>
<td>146</td>
<td>4.87±5.12</td>
</tr>
<tr>
<td>Pocket seroma/hematoma requiring surgical intervention</td>
<td>3</td>
<td>0.10</td>
<td>8</td>
<td>0.26</td>
<td>29</td>
<td>9.67±9.61</td>
</tr>
<tr>
<td>Pocket/ICD infection</td>
<td>20</td>
<td>0.68</td>
<td>25</td>
<td>0.81</td>
<td>413</td>
<td>20.65±18.93</td>
</tr>
<tr>
<td>Upgrade from ICD to CRT/ICD</td>
<td>45</td>
<td>1.52</td>
<td>0</td>
<td>0.00</td>
<td>141</td>
<td>3.13±2.99</td>
</tr>
<tr>
<td>Other device related</td>
<td>17</td>
<td>0.58</td>
<td>27</td>
<td>0.88</td>
<td>203</td>
<td>11.94±19.20</td>
</tr>
</tbody>
</table>

Other device related includes hemothorax/pneumothorax, pocket erosion, loose set screw, pulse generator migration, pocket seroma/hematoma requiring observation, or prophylactic lead replacement. CRT indicates cardiac resynchronization therapy; ICD, implantable cardioverter-defibrillator; LV, left ventricular; NA, not applicable because of no events or only 1 event; and PYR, patient-year at risk.
Conclusion
In RAFT, the use of CRT significantly reduced hospitalization rates for all cause, cardiovascular, and HF indications and reduced the overall average length of hospital stay.

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References


CLINICAL PERSPECTIVE

Cardiac resynchronization therapy (CRT) has been shown to reduce hospitalizations for heart failure (HF) in patients with mild to moderate HF. We report a detailed analysis of the causes of hospitalization, hospitalization rates, and hospitalization lengths of stay in patients randomized to implantable cardioverter-defibrillator (ICD) or ICD-CRT in the Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT). At the 18-month follow-up, the proportion of patients hospitalized at least once for HF was significantly lower in the ICD-CRT group (11.3%) compared with the ICD group (15.6%; P=0.003). The proportions of patients hospitalized for a device-related indication were similar in the ICD-CRT group (16.4%) and ICD group (13.9%; P=0.148). The number of hospitalizations for any cause (n=1448 versus n=1553; P=0.042), any cardiovascular cause (n=667 versus n=790; P=0.017), and any HF cause (n=385 versus n=505; P<0.0001) was significantly lower in ICD-CRT group compared with the ICD group, whereas the number of hospitalizations for device-related causes was significantly higher in the ICD-CRT group compared with the ICD group (n=246 versus n=159; P<0.001). Although, the reduction in hospitalizations for HF in the CRT-ICD group was offset by an increased number of hospitalizations for device-related indications, the length of hospital stay for any cause was significantly lower in the ICD-CRT group (8.83±13.30 days) compared with the ICD group (9.59±14.40 days; P=0.005). The reduction in total number of hospitalizations and length of stay per hospitalization should translate into cost savings for healthcare systems, but this will require further analysis.

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