Variation in daily median respiratory rate identifies patients at higher risk of worsening HF in 30 days

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Presenter Disclosure Information

• I have financial relationships to disclose:
  • Employee of:
  • Consultant for: Boston Scientific
  • Stockholder in:
  • Research support from: Boston Scientific
  • Honoraria from:
Introduction

- Respiratory distress is common in heart failure (HF) patients and is the primary driver for HF hospitalization.
- Respiratory symptoms such as breathlessness and orthopnea are significantly related to increased mortality and hospitalization.
- Many HF patients have an implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy defibrillator (CRT-D), which is capable of monitoring respiration via intra-thoracic impedance.
- The Multisensor Chronic Evaluations in Ambulatory Heart Failure Patients (MultiSENSE) study collects respiratory data in HF patients, enabling evaluation of prognostic value of the Respiratory Rate Trend (RRT).
Study Design

- MultiSENSE study is a multi-center, non-randomized, feasibility study to evaluate the ability of multiple sensors to reflect early signs of worsening heart failure
- Up to 990 subjects with existing devices
- Key inclusion criteria:
  - Age 18 or above
  - Currently implanted with a COGNIS CRT-D system
  - NYHA Class II, III or IV within the last 6 months
- Key exclusion criteria:
  - Documented as pacemaker dependent
  - A history of appropriate tachycardia therapy within 1 week prior to enrollment
  - Likely to undergo lead or PG revision
  - Subjects that have received a heart or lung transplant
  - Receiving mechanical circulatory transplant
  - A life expectancy of less than 12 months
HF Event Definition

- A HF event is declared when the patient has signs and/or symptoms consistent with congestive HF and
  - receives unscheduled intravenous decongestive therapy that does not involve formal in-patient hospital admission, regardless of the setting, or,
  - is admitted for HF and receives an augmented HF regimen with oral or intravenous medications.

- HF events were reported by centers and adjudicated by an internal employee who is blinded to sensor data and independent of study analysis.
Respiratory Rate Trends

• The device is capable of trending daily maximum, median and minimum RR up to a year.
• Daily Maximum Respiratory Rate
  • Maximum of medians of all 10-minute epochs in 24 hours
  • Capture a period of fast breathing, e.g., exercise
• Daily Median Respiratory Rate
  • Median of all valid breaths in 24 hours
• Daily Minimum Respiratory Rate
  • Minimum of medians of all 30-minute epochs in 24 hours
  • Capture a period of slow breathing, e.g., sleeping
Method

- Daily maximum, median and minimum RRTs were collected using an investigational device based on the COGNIS® CRT-D device.
- Differences in respiratory rates between the 10th and 90th percentiles (10%-90% range) were calculated using data in evaluation periods every month.

Whole follow-up period of a patient:

- Enrollment
- 1st monthly evaluation
- 2nd monthly evaluation
- 3rd monthly evaluation
- Repeat as needed until end of follow-up
Method

- Patients were classified into two groups depending on the RRT range: high variation (range > 4 breaths/minute) and low variation (range ≤ 4).

- Cox proportional hazard model was used to determine the risk and to estimate the hazard ratios (HR, 95% confidence interval (CI)) of a HF event in the next 30-day window in each group.
## Patient Demographics

<table>
<thead>
<tr>
<th></th>
<th>ALL (161)</th>
<th>Patients with HF event (31)</th>
<th>Patients without HF event (130)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs</td>
<td>66.8</td>
<td>64.7</td>
<td>67.3</td>
<td>0.243</td>
</tr>
<tr>
<td>Sex (% Male)</td>
<td>72</td>
<td>76</td>
<td>74</td>
<td>1</td>
</tr>
<tr>
<td>NYHA I / II / III /IV %</td>
<td>8/57/33/0</td>
<td>7/38/52/0</td>
<td>9/61/29/0</td>
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<tr>
<td>LVEF</td>
<td>26.7</td>
<td>22.9</td>
<td>27.4</td>
<td>0.048</td>
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<tr>
<td>Weight lbs</td>
<td>197</td>
<td>203</td>
<td>195</td>
<td>0.64</td>
</tr>
<tr>
<td>Ischemic %</td>
<td>53.2</td>
<td>69</td>
<td>50</td>
<td>0.1</td>
</tr>
<tr>
<td>BMI</td>
<td>29.4</td>
<td>30.3</td>
<td>29.3</td>
<td>0.62</td>
</tr>
<tr>
<td>DCM %</td>
<td>50.9</td>
<td>52</td>
<td>54</td>
<td>1</td>
</tr>
<tr>
<td>MI %</td>
<td>37.9</td>
<td>41</td>
<td>40</td>
<td>1</td>
</tr>
<tr>
<td>COPD %</td>
<td>14.9</td>
<td>17</td>
<td>15</td>
<td>0.78</td>
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<tr>
<td>Asthma %</td>
<td>11.2</td>
<td>17</td>
<td>10</td>
<td>0.33</td>
</tr>
<tr>
<td>Diabetes %</td>
<td>38.5</td>
<td>52</td>
<td>38</td>
<td>0.21</td>
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<tr>
<td>Renal Dx %</td>
<td>24.2</td>
<td>45</td>
<td>21</td>
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<tr>
<td>Hypertension %</td>
<td>23.7</td>
<td>15</td>
<td>26</td>
<td>0.22</td>
</tr>
<tr>
<td>SDB %</td>
<td>15.5</td>
<td>34</td>
<td>12</td>
<td>0.009</td>
</tr>
<tr>
<td>ACE %</td>
<td>61</td>
<td>45</td>
<td>64</td>
<td>0.065</td>
</tr>
<tr>
<td>BB %</td>
<td>92</td>
<td>87</td>
<td>93</td>
<td>0.29</td>
</tr>
<tr>
<td>DIUR %</td>
<td>79</td>
<td>93</td>
<td>75</td>
<td>0.027</td>
</tr>
</tbody>
</table>
Results

- Significant separation in 30-day risk of HF events was observed between patient groups using daily median RRT.
- Patients with a higher 30-day variation in daily median RRT had 4.9-fold increased risk of HF hospitalization within the next month (HR (95% CI): 4.9 (2.2 – 11), p<0.001).
- The risk remained high (HR (95% CI): 5.9 (2.5 – 14), p<0.001) after adjusting for key clinical variables (age, gender, NYHA and LVEF).
Conclusion

• Initial data from the MultiSENSE study indicates that patients with higher 30-day variation in daily median RRT have a higher risk of experiencing worsening HF in the next month.
• Further evaluation is warranted to determine its clinical value in HF patient management.