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Stratifying patients at the risk of heart failure hospitalization using existing device diagnostic thresholds

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ABSTRACT

Background: Heart failure hospitalizations (HFHs) cost the US health care system ~$20 billion annually. Identifying patients at risk of HFH to enable timely intervention and prevent expensive hospitalization remains a challenge. Implantable cardioverter defibrillators (ICDs) and cardiac resynchronization devices with defibrillation capability (CRT-Ds) collect a host of diagnostic parameters that change with HF status and collectively have the potential to signal an increasing risk of HFH. These device-collected diagnostic parameters include activity, day and night heart rate, atrial tachycardia/atrial fibrillation (AT/AF) burden, mean rate during AT/AF, percent CRT pacing, number of shocks, and intrathoracic impedance. There are thresholds for these parameters that when crossed trigger a notification, referred to as *device observation*, which gets noted on the device report. We investigated if these existing device observations can stratify patients at varying risk of HFH.

Methods: We analyzed data from 775 patients (age: 69 ± 11 year, 68% male) with CRT-D devices followed for 13 ± 5 months with adjudicated HFHs. HFH rate was computed for increasing number of device observations. Data were analyzed by both excluding and including intrathoracic impedance. HFH risk was assessed at the time of a device interrogation session, and all the data between previous and current follow-up sessions were used to determine the HFH risk for the next 30 days.

Results: 2276 follow-up sessions in 775 patients were evaluated with 42 HFHs in 37 patients. Percentage of evaluations that were followed by an HFH within the next 30 days increased with increasing number of device observations. Patients with 3 or more device observations were at 42× HFH risk compared to patients with no device observation. Even after excluding intrathoracic impedance, the remaining device parameters effectively stratified patients at HFH risk.

Conclusion: Available device observations could provide an effective method to stratify patients at varying risk of heart failure hospitalization.

Introduction

Implantable cardioverter defibrillator (ICD) and cardiac resynchronization therapy (CRT) devices have become the mainstay of treating persistent systolic heart failure in addition to guideline directed medical therapy.[1,2] Many of these devices are implanted in patients with congestive heart failure with New York Heart Association (NYHA) class status of II to IV. While these devices considerably ameliorate patient morbidity and mortality, heart failure remains a significant economic burden costing the US health care system ~$30 billion annually. Heart failure

Abbreviations: AF, atrial fibrillation; AT, atrial tachycardia; CRT, cardiac resynchronization therapy; EF, ejection fraction; GEE, generalized estimating equation; HF, heart failure; HFH, heart failure hospitalization; HRV, heart rate variability; ICD, implantable cardioverter defibrillator; NHR, night heart rate; NYHA, New York Heart Association; VRAF, ventricular rate during AF.

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hospitalizations (HFHs) account for two-thirds of the total expense.[3] Identifying patients at risk of worsening heart failure to allow timely intervention has the potential to prevent hospitalizations and improve long-term patient outcomes while reducing costs of care.

In addition to providing life-saving therapies, implantable devices collect a host of continuous physiological patient data (e.g. activity, day and night heart rate, AT/AF burden, heart rate during AT/AF, percent CRT pacing, number of shocks, and intrathoracic impedance). However, the data collected vary by manufacturer. For example, not all manufacturers have devices with intrathoracic impedance capability. Also, while all devices include a single or multi-axis accelerometer, proprietary algorithms to derive daily activity from accelerometer signals vary (see Methods for details). Many of the diagnostic variables have been shown to be prognostic markers of worsening heart failure and/or mortality risk. For example, NHR is a marker of autonomic tone, and an elevated NHR is associated with higher HFH risk.[4] Activity is a reflection of patient functional capacity, and decreasing activity is associated with worsening HF status.[4–7] A loss of CRT pacing compromises cardiac hemodynamics and hence leads to worsening patient status.[8] And finally, a decrease in intrathoracic impedance is associated with an increase in wedge pressure, elevated pre-load, and risk of fluid extravasation into the lungs.[9] Risk stratification models combining various device diagnostic parameters have been proposed.[10–12] The diagnostic performance of these models is better than each parameter alone. However, the clinical adoption of these risk stratification models has been slow because they use thresholds and measurement schemes not yet implemented in the implantable devices. Some of these approaches in fact use a fixed 30-day look back window requiring manual sifting of data to identify trends, thus making it cumbersome to use them in day-to-day practice.

All CRT-D devices have thresholds for various parameters that when crossed trigger a notification, referred to as *device observation*. The purpose of this study was to examine the performance of the existing device observations for stratifying patients at HFH risk. Since the impedance observation is not available in all devices [e.g. OptiVol observation is not available on CareLink (Medtronic Inc. MN) in the US], we performed the analysis with and without impedance observation. Furthermore, we investigated the relationship between the number of device observations triggered and risk of HFH.

Methods

We performed retrospective analysis using patient data from FAST[13] and PARTNERS-HF[10] clinical trials using Medtronic devices. Both study protocols were approved by institutional review boards and all patients provided written informed consent. FAST was a prospective double-blinded observational study in CRT-D and ICD patients ($n = 109$) with EF $\leq$ 35% and NYHA class III or IV. PARTNERS-HF was a prospective observational study in CRT-D patients ($n = 1024$) with EF $\leq$ 35%, NYHA class III or IV, and QRS duration $\geq$130 ms. The two studies combined had 1133 patients and 220 HFHs. Only patients with an OptiVol capable CRT-D device were included in this analysis. Follow-up sessions with less than 7 days of data before and less than 30 days of data after the evaluation were excluded. Furthermore, if there was another follow-up session within 30 days of a previous session, the second session was excluded. After applying above criteria, 186 HFHs in 775 patients and a total of 2276 follow-up sessions were available for analysis. Mean follow-up was 13 $\pm$ 5 months. HFH associated with signs and symptoms of pulmonary congestion was used as the endpoint. All HFHs were adjudicated by an independent committee. The HFH event rate of 22.2% per year in this cohort is comparable to that in NYHA III and IV device patients.[14,15]

Diagnostic parameters and thresholds

The following diagnostic parameters in Medtronic devices have an observation: OptiVol index, AT/AF burden, ventricular rate during AT/AF (VRAF), activity, night heart rate (NHR), and percent pacing (% CRT pacing) (Fig. 1). In addition, an observation is noted if defibrillation shocks are delivered and this was also included in our analysis. Briefly, the measurement scheme for various parameters was as follows. Impedance (Z) is measured intrathoracically across the right ventricular (RV) coil and device-can by injecting a small current pulse (I) and measuring the developed voltage (V; $Z = I/V$). OptiVol index is derived as the cumulative difference between expected and actual Zs for the duration when expected Z is higher than actual Z. When actual Z exceeds expected Z, OptiVol index is set to zero. Since OptiVol index is integration of Z over certain duration, it is measured in units of ohm-days (Ω-days). A higher value of OptiVol index has been shown to be associated with HFH.[9] Several electrophysiological parameters including NHR, AF burden, and VRAF are derived from atrial and ventricular electrograms (egms) acquired by the device at 10 ms resolution. Device algorithms, such as PR Logic,[16] are applied to discriminate among different rhythms and derive these electrophysiological parameters. NHR is the average heart rate between midnight and 4 am and is a measure of resting heart rate. AF burden is measured as total duration of fast atrial rate during a 24-h period associated with atrio-ventricular conduction ratio $\geq$2:1. VRAF is the average ventricular rate during AF over a 24-h duration. Activity is a quantitative measure of active duration and is a surrogate of functional capacity. It is measured by a single axis accelerometer in the device that is used to detect patient motion and convert it into discrete electrical signals. An algorithm then converts these electrical signals to number of minutes active for the entire 24-h duration during a day (day and night time activities are not reported separately), where a minute is considered active if accelerometer registers signal equivalent to 70 steps/min or greater.[4] The device recorded activity has been shown to have a strong intra-individual correlation with activity measured using a validated external sensor.[5] However, details of the algorithm differ between implantable and external devices (e.g. pedometers and external accelerometers) and absolute duration of reported activity between the two may differ.

All of the above parameters have a threshold value, which when exceeded triggers a device observation. Fig. 1 shows empirically derived nominal threshold values for various parameters that can be tailored on a patient basis. All nominals (or values close to the nominals) have been shown to be associated with greater HFH or mortality risk. An OptiVol observation is noted on the device report when a value of 60 Ω-days is exceeded, a threshold shown to predict HFH with optimal sensitivity and false alert rate.[9] AT/AF burden of $\geq$6 h/day for at least one day within the last 30-days is associated with 2$\times$ risk of an HF event.[17] This risk is further exacerbated with poor rate control with V-rate $>$ 90 bpm.[17] NHR of $>$90 bpm discriminates between hospitalized and non-hospitalized patients.[18] And finally, CRT pacing $<$90% is associated with increased mortality.[19]

The availability of OptiVol observations varies by geography and mode of device interrogation. For example, while there is an OptiVol observation on the programmer report in the United States, no such observation exists on the CareLink HF management report. Outside the United States, the OptiVol observation is available in both the programmer and CareLink reports. Thus, we performed our analysis by both including and excluding the OptiVol observation.