Achieving Guideline Directed Heart Rate Control Early Post-hospitalization

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ABSTRACT

Guidelines for the treatment of heart failure (HF) recommend the titration of beta-blockers (BB) to a target dosage shown to be effective in clinical trials. The benefit of BBs is associated with heart rate (HR) control, with a target resting HR<70 bpm which in clinical trials have been associated with improved clinical outcomes. The primary purpose of this study was to gauge the ability to achieve guideline-directed medical therapy HR control in the early post-hospitalization period for HF patients with the wearable cardioverter defibrillator (WCD), assessing whether the WCD could be used to evaluate HR both at rest and during activity to determine if targets were being met and to adequately direct clinical decision making. The WCD platform allows continuous recording of HR. To assess the guideline-directed therapy goals for reduction of resting HR, HR was evaluated both at rest (nighttime: midnight-7am; daytime: 7am-midnight), and during activity of daily living. HR data during activity of daily living (ADL) and rest were collected from patients with HF that wore the WCD for ≥ 5 weeks (n=1353) between 2015 and 2017. First, 643,891 activity episodes from 1,353 patients were analyzed. Daytime and nighttime resting HRs significantly dropped from beginning to end of WCD use (day: 72.5 bpm vs. 69.0 bpm, p<0.0001; night: 68.1 vs. 64.3, p<0.0001). However, 43% of patients still had an average daytime resting HR ≥70 bpm during the last week of WCD use. When comparing an individual's peak activity HR during the first week of WCD use to the last week, there was no difference (93.6 bpm vs. 94.1 bpm, p=0.23). During ADL, 31% of patients had a HR ≥100 bpm, 14% of patients had a HR ≥110 bpm, and 6% had a HR ≥120 bpm. In conclusion, months after hospital discharge, 43% of patients did not meet guideline-directed resting target HR control, indicating they may not have been effectively managed with BB. HR during ADL may have also been higher than preferred. Remote HR monitoring may help physicians to adequately titrate guideline directed medical therapy, thus improving clinical outcomes in HF patients.

Keywords: Heart failure, wearable cardioverter defibrillator, heart rate, guideline directed medical therapy, beta-blockers

INTRODUCTION:

HR is a marker of sympathetic and parasympathetic activities, and a higher resting HR may be a sign of autonomic dysfunction associated with heart failure (HF)[1,2]. HR is inversely related to mortality, regardless of known cardiac disease, with a reported 14% increase in cardiovascular death for every 10 bpm increase in HR in the general population.[3] Nighttime resting HR may be even more predictive of all-cause mortality and cardiac events.[4] Beta-blockers (BB) are standard therapy for patients with heart failure with reduced ejection fraction (HFrEF), and the benefit is, in part, due to lowering HR. In patients with HFrEF, a lower resting HR is associated with lower all-cause mortality, particularly for those in sinus rhythm.[5] Although the heart failure guidelines focus on achieving adequate dosages shown to be effective in clinical trials (usually the highest doses as possible); actual HR is clinically used during the optimization period to advance dosage. Further, HF guidelines also recommend the use of ivabradine in patients already on maximum tolerated doses of BB who are in sinus rhythm with a resting HR of ≥70 BPM.[6,7] The wearable cardioverter defibrillator (WCD), typically used for the monitoring and treatment of harmful ventricular tachyarrhythmias, also provides remote HR monitoring. We hypothesized that resting HR derived from the WCD may be a direct measure of whether patients in the early post-discharge period are being adequately treated with BBs or ivabradine. Our objective was to determine if WCD recordings provided a feasible method to assess resting HR as well as HR during activity of daily living (ADL) in order to determine if guideline-directed HR targets are being achieved in HF patients post-hospitalization.

METHODS:

This was a retrospective study for determination of resting HR and HR during activity in patients with HF. All subjects provided consent to use their data for quality monitoring and research. The study

was performed in agreement with good clinical practice guidelines and with the standards established for human experimentation by the Declaration of Helsinki.

All European patients with heart failure or myocardial infarction with a low EF and prescribed the continuous monitoring enabled WCD for ≥ 5 weeks (n=1353), with valid activity and resting HR available, and had a known outcome of either death, ICD implantation, or EF improvement, between 2015 and 2017 were included in this retrospective analysis. This cohort represented approximately 23% of the entire WCD patient population (approximately 6,000) during this time period.

The WCD (LifeVest®, ZOLL, Pittsburgh, PA, USA) automatically detects and treats sustained ventricular tachycardia (VT) and ventricular fibrillation (VF). A detailed description of the WCD has been provided in prior publications and reviews.[8-10] The WCD platform also allows for continuous recording of HR, activity, and body position via the ECG electrodes and a 3-axis accelerometer in the electrode belt. Only episodes with clean ECG data (no artifact) were used for collecting HR data. Second by second HR was calculated from the recorded continuous monitoring data.

Rest was defined as a ≥30 minute period where the device accelerometer recorded <60 milligravity (mG). Daytime was defined as being from 07:00 am to midnight and nighttime from midnight to 07:00 am. Activity of daily living (ADL) episodes were defined as a contiguous period (≥ 60 secs) where the device accelerometer records a ≥ 60 mG mean amplitude deviation. Two such periods split by a gap shorter than 10 seconds were treated as a single contiguous period. Peak HR was defined by the 90th percentile of HRs during activity.

Resting HRs are reported as weekly medians. The percentage of patients below the 70 bpm (guideline recommended threshold) and also below 90 bpm was analyzed. [6,7] The 90 bpm resting HR threshold was chosen to represent a “very high” resting HR.

The percentages of patients with significantly elevated HR during ADL were analyzed. Exercise therapy guidelines recommend the HR not exceed 20-30 BPM above resting HR.[11,12] HRs that were ≥100 bpm were divided into groups according to a HR increase of each 10 bpm.

To determine whether resting HR was being well-controlled in these patients post-hospitalization, and whether it improved over time with therapy, HR was compared from the first week of WCD use (BOU) to the last week of WCD use (EOU).

Descriptive statistics were used to summarize the datasets. Categorical variables were expressed as numbers and percentages. All continuous variables are reported as mean ± standard deviation, or medians for non-parametric data. A paired T-Test was performed to determine differences between HR during the first week of use (beginning of use: BOU) and the last week of use (end of use: EOU). A T-Test between two different populations was used determine differences between HR during the ADL at BOU/EOU. Data were considered statistically significant with a 2-sided p value ≤0.05.

RESULTS:

There were 1,353 patients who met inclusion criteria for analysis of resting HR and HR during ADL (Table 1). Patients were prescribed and indicated for the WCD due to a low EF (≤ 35%), primarily from HF or post-myocardial infarction (MI) with percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). They wore the WCD for a median 21.2 hr/day over a median period of use of 73 days.

Both the daytime and nighttime resting mean HRs dropped significantly from beginning to end of WCD use (day: 72.5 bpm vs. 69.0 bpm, $p<0.0001$; night: 68.1 vs. 64.3, $p<0.0001$)(Figure 1). When comparing daytime and nighttime resting HR, there was a slowing down of approximately 4-5 bpm at

nighttime, both at the BOU and EOU (each p <0.0001). At the BOU, 55% and 40% of patients were ≥ 70 bpm at rest during the daytime or nighttime, respectively (Figure 2). By the EOU, these numbers were 43% and 28% during the daytime or nighttime, respectively. Regardless of time of day, less than 10% of patients had a resting HR ≥ 90 bpm at the BOU, reduced by half by the EOU.

From the 1,353 patients, a total of 643,891 activity episodes were analyzed. The mean HR during ADL did not change from the BOU to EOU (93.6 bpm vs 94.1 bpm, respectively, p=n.s.)(Figure 3). During the first week and last week of WCD use, activity HR was ≥100 bpm in 30% and 31% of patients, respectively. 6% of patients had a peak activity HR that was ≥ 120 bpm and 3% a peak activity HR >130 bpm at either BOU or EOU (Figure 4).

DISCUSSION:

The current study analyzed a large cohort of patients wearing the WCD for HF with a low EF. Over the WCD prescription time, both daytime and nighttime HR decreased significantly. However, a significant percentage, 42% at daytime and 28% at nighttime, revealed resting HRs higher than 70 bpm thus, greater than the guideline-directed target. Conversely, HR during activity showed no significant difference from early after hospital discharge to 2 to 3 months later.

The WCD is primarily useful for detecting and treating ventricular tachyarrhythmias. However, the most recent WCD platform also allows for continuous recording of HR, activity and body position via the ECG electrodes and a 3-axis accelerometer in the electrode belt. There are currently no published studies available investigating the diagnostic usefulness of the continuous WCD HR monitoring. The current study was able to illustrate that in patients utilizing the WCD, resting HRs could be reliably measured. Moreover, the WCD was also able to detect and measure the HR during activity of daily living and during directed exercise. Therefore, the WCD may have, in addition to the basic function of preventing sudden cardiac death, an additional advantage in the management of heart failure patients

in optimizing guideline directed medical therapy at the time of prescription. Further studies are needed to investigate this additional value of the WCD, especially regarding optimization of GDMT and thereby possibly reducing the need for final ICD implantation. Surprisingly, significant gaps continue to exist in use of GDMT for HFrEF despite numerous national quality improvement efforts (IMPROVE-HF).[13,14] Recently, it has been demonstrated that the use of WCD improves GDMT in patients with HFrEF [15]. The current study extends this work and demonstrates the value of WCD use as a monitoring tool early post-discharge to optimize GDMT. While using the WCD to monitor and report HR after a heart failure event can be directly used to adjust BB therapy, it may also serve as a reminder to the healthcare professionals to also assess the titration of other pharmacologic agents included in optimal guideline directed medical therapy.

The current study demonstrated the ability of the WCD diagnostic capability to measure resting HRs. Moreover, between the beginning and the end of WCD use, a significant decrease in resting HRs was detected, which was evident during both daytime and nighttime. Temporal changes in HR, such as between doctor visits, are also predictive of outcomes in HF patients. [16] The magnitude of HR reduction plays an important role in the mortality benefit of BB. A meta-analysis looking at 23 BB trials found that for every resting HR reduction of 5 BPM with BB, there was an 18% reduction in the risk of death.[19] While HR reduction may not be the only mechanism by which BB provide mortality benefit, it can at least be viewed as a marker or measure of BB response. The importance of HR control is also supported by more recent studies with ivabradine, a newer therapeutic agent that works specifically by lowering HR in patients not effectively treated by BB. It appears that in patients with HFrEF taking both BB and ivabradine, that the magnitude of HR reduction is more important to outcome than the dose of BB.[17] HR reduction is also significantly correlated with LVEF improvement with both BB and ivabradine.[18,19]

The current study displays that at the end of WCD use 40% of patients at daytime and 28% at nighttime still had HRs >70 bpm. Despite the limitations of this study (the actual rhythm of the patient

was unknown, WCD indication was not recorded in some patients, and there was no information regarding BB or ivabradine usage), it may be speculated that while a relevant proportion of the study cohort may have received an optimization of heart failure therapy, another large proportion of patients could be in need of further optimization to meet the HRHR target of ≤70 bpm.

HF guidelines recommend the use of maximum tolerated doses of BB. Further, ivabradine should be added in patients already on maximum BB dosage, who are in sinus rhythm with a resting HR of ≥70 BPM.[6,7] Thus, the WCD may be an important tool in directing heart failure therapy. Also, the WCD may help to clarify more important questions, especially regarding the optimal HR target in atrial fibrillation and if there are differences in daytime and nighttime HRs.

Guidelines recommend a target resting HR <70 bpm.[6,7] Currently, the guidelines do not distinguish between daytime and nighttime. Further, the guidelines recommend only a target resting HR but no target activity HR. The current study reports on both resting HR and HR during activity with the WCD. Therefore, we propose an additional benefit of the WCD as diagnostic tool, beside its function as prevention of sudden cardiac death. We propose that weekly measurements of resting HR may help to prompt optimization of GDMT. Therefore, further evaluation of the diagnostic features of the WCD is warranted to determine its effect on GDMT and cardiovascular endpoints like mortality.

This analysis did not document the patient's actual rhythm at all points of heart rate determination. Atrial fibrillation with an uncontrolled ventricular response could have accounted for some high heart rates, but those rates would still suggest lack of GDMT HR control. The WCD indication was not recorded in some patients. Since this was a retrospective observational study, the prescription, compliance, and dosage of BB or ivabradine usage was not collected. However, the use of real HR data may ultimately prove to be a superior method than collecting information from discharge summaries or

pharmacy claims data. Future prospective studies utilizing the WCD in patients with HFrEF should consider linking additional datasets to validate appropriate medication use and adherence.

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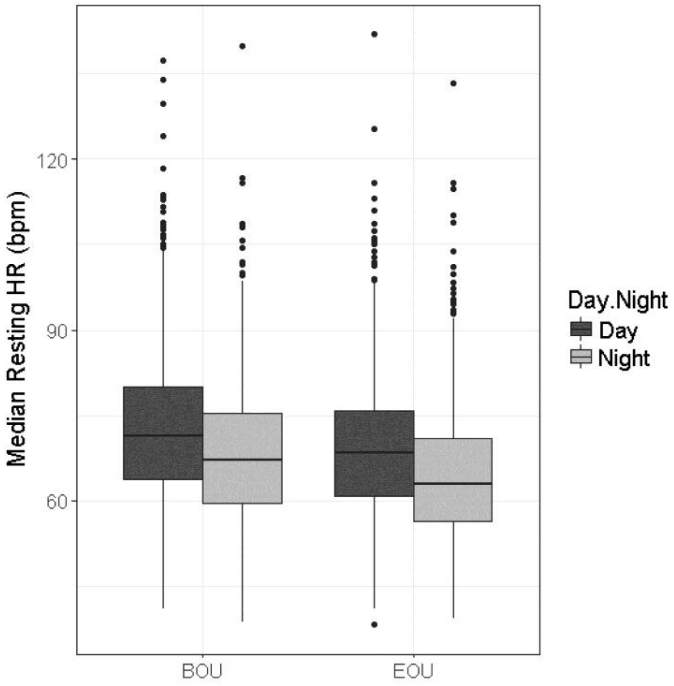
TABLES and FIGURES



		Mean ± SD
BOU	Day	72.5 ± 12.3
BOU	Night	68.1 ± 12.0
EOU	Day	69.0 ± 11.5
EOU	Night	64.3 ± 11.3

p<<0.0001
p<<0.0001
p<<0.0001
p<<0.0001

Figure 1. Average resting HR at the beginning (BOU) and end of use (EOU)

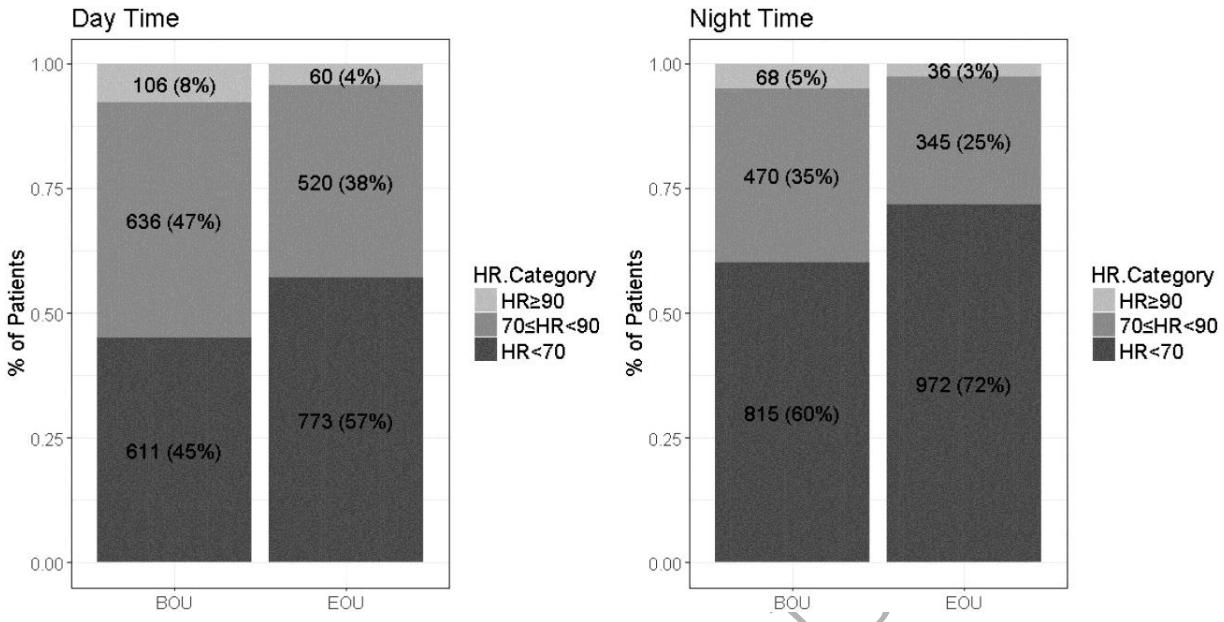
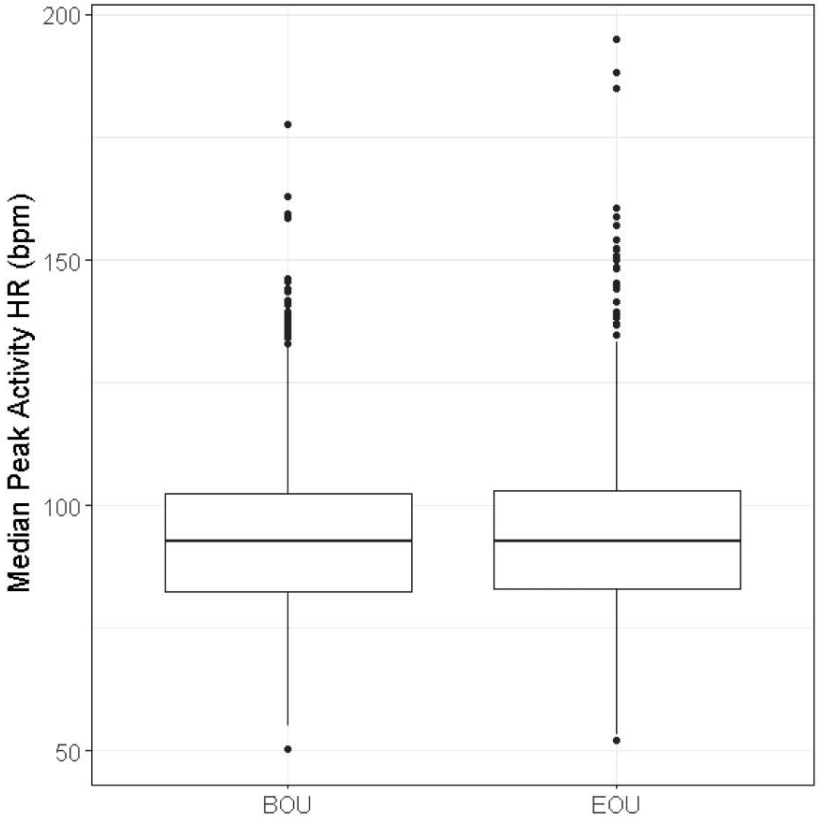


Figure 2. Percentage of patients with resting HR below the thresholds of 70 bpm or 90 bpm at the beginning (BOU) and end of use (EOU).



	Mean ± SD
BOU	93.6 ± 16.2
EOU	94.1 ± 16.3

p = 0.2322
(paired t-test)

Figure 3. Average HR during Activity of Daily Living (ADL) at the BOU and EOU

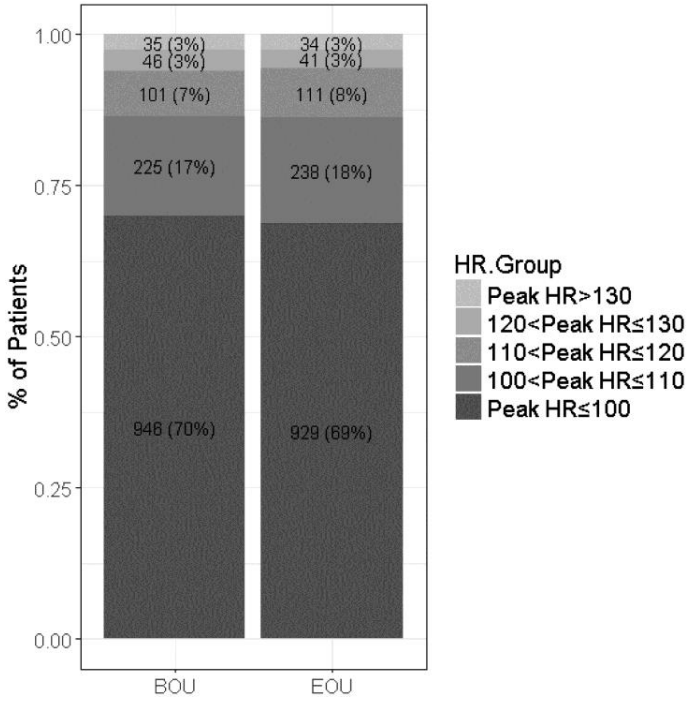


Figure 4. Percentage of patients with peak activity HR above 100 bpm at the beginning (BOU) and end of use (EOU).

Table 1. Patient Characteristics for Group 1 (N=1353)

Variable
Median Age [IQR] (years) 58 [50 - 67]
Male 1085 (80%)
Median Length of use (days) 73 [53 - 91] **[IQR]**
of activities 643,891
Diagnoses
CHF 614 (45%)
PCI/CABG/MI 537 (40%)
Myocarditis 81 (6%)
Heart transplant 4 (<1%)
Others 117 (9%)

CHF: congestive heart failure; PCI: percutaneous coronary intervention; CABG: coronary artery bypass graft; MI: myocardial infarction