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QUARTERLY FOCUS ISSUE: HEART FAILURE

Combined Heart Failure Device Diagnostics Identify Patients at Higher Risk of Subsequent Heart Failure Hospitalizations

Results From PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) Study

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Objectives We sought to determine the utility of combined heart failure (HF) device diagnostic information to predict clinical deterioration of HF in patients with systolic left ventricular dysfunction.

Background Some implantable devices continuously monitor HF device diagnostic information, but data are limited on the ability of combined HF device diagnostics to predict HF events.

Methods The PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) was a prospective, multicenter observational study in patients receiving cardiac resynchronization therapy (CRT) implantable cardioverter-defibrillators. HF events were independently adjudicated. A combined HF device diagnostic algorithm was developed on an independent dataset. The algorithm was considered positive if a patient had 2 of the following abnormal criteria during a 1-month period: long atrial fibrillation duration, rapid ventricular rate during atrial fibrillation, high (≥60) fluid index, low patient activity, abnormal autonomics (high night heart rate or low heart rate variability), or notable device therapy (low CRT pacing or implantable cardioverter-defibrillator shocks), or if they only had a very high (≥100) fluid index. We used univariate and multivariable analyses to determine predictors of subsequent HF events within a month.

Results We analyzed data from 694 CRT defibrillator patients who were followed for 11.7 ± 2 months. Ninety patients had 141 adjudicated HF hospitalizations with pulmonary congestion at least 60 days after implantation. Patients with a positive combined HF device diagnostics had a 5.5-fold increased risk of HF hospitalization with pulmonary signs or symptoms within the next month (hazard ratio: 5.5, 95% confidence interval: 3.4 to 8.8, $p < 0.0001$), and the risk remained high after adjusting for clinical variables (hazard ratio: 4.8, 95% confidence interval: 2.9 to 8.1, $p < 0.0001$).

Conclusions Monthly review of HF device diagnostic data identifies patients at a higher risk of HF hospitalizations within the subsequent month. (PARTNERS HF: Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure; NCT00279955). (J Am Coll Cardiol 2010;55:1803–10)

Despite numerous therapeutic advances, patients with heart failure (HF) are at a high risk of mortality and morbidity. HF accounts for 7% of all Medicare admissions, and in

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Abbreviations and Acronyms

CI = confidence interval
HF = heart failure
ICD = implantable cardioverter-defibrillator
CRT = cardiac resynchronization therapy
CRT-D = cardiac resynchronization therapy and defibrillator
HCU = health care utilization
HR = hazard ratio
NYHA = New York Heart Association

2008, HF inpatient costs were approximately $18.8 billion (1,2). The ability to predict which patients will subsequently be hospitalized for HF is limited. Traditional evaluative measures such as physical signs and symptoms are poorly associated with hemodynamics and are typically only assessed intermittently; consequently, they may not identify patients in time for intervention to prevent imminent adverse events.

Implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy and defibrillator (CRT-D) are recommended by practice guidelines as a class I therapy for a large number of HF patients based on clinical trial evidence showing a significant reduction in hospitalization and mortality with their use (3,4). Expert consensus has recognized the utility of reviewing the HF device diagnostic information from these devices, and the CPT (Current Procedure Terminology) codes now include review of the HF device diagnostics in person or remotely at monthly intervals (5).

Previous studies have demonstrated the ability of individual pieces of HF device diagnostic data, such as hemodynamics (pressure or fluid index derived from intrathoracic impedance) or autonomics to predict HF events and/or change outcomes (6–9). Some investigators have observed close associations between changes in individual HF device diagnostics and HF events (7). Preliminary review suggests that combining HF device diagnostic data into a single algorithm may improve the overall ability to risk-stratify HF patients. However, the clinical utility of an algorithm that combines multiple HF device diagnostic parameters has not been investigated.

The PARTNERS HF (Program to Access and Review Trending Information and Evaluate Correlation to Symptoms in Patients With Heart Failure) was a prospective, nonrandomized, multicenter observational study designed to determine the potential utility of combined HF device diagnostic information to predict the clinical deterioration of ambulatory HF patients when reviewed at routine follow-up intervals. The primary hypothesis of the study was that combining HF device diagnostic data would enhance the ability to risk-stratify patients for subsequent HF events.

Methods

Study patients. The design of the PARTNERS HF Study was described in a previous publication (10). The key patient inclusion criteria were a left ventricular ejection fraction ≤35%, New York Heart Association (NYHA) functional class III or IV, intrinsic QRS duration ≥130 ms, and use of a commercially available CRT-D system (Medtronic Models 7297, 7303, 7277, 7289, or C154DWK; Medtronic Inc., Minneapolis, Minnesota). The key exclusion criteria were acute coronary intervention within the past month, permanent atrial arrhythmias, a history of heart transplantation, and end-stage renal disease requiring dialysis.

This observational trial was undertaken at 100 sites throughout the U.S. Enrollment began in June 2004 and ended in February 2007, with follow-up completed in April 2008. The study was approved by the institutional review board at each participating institution. All patients provided informed consent.

Study design and event definitions. Patients were followed for 12 months after enrollment (defined as implantation date or consent date, whichever occurred later). Standard clinical evaluations occurred at 3, 6, 9, and 12 months after enrollment. At each follow-up visit, the following information was collected: NYHA functional classification, American College of Cardiology/American Heart Association stage A through D classification, and patient cardiovascular medications. Additionally, each patient's CRT-D memory was interrogated to retrieve the HF device diagnostic data, which were then stored in a database for subsequent analysis.

Throughout the study, data on all cardiovascular-related adverse events and deaths were collected. All adverse events and deaths were independently adjudicated by the Adverse Event Advisory Committee. This committee classified each adverse event as cardiovascular or not cardiovascular and adjudicated the event as HF related only if it resulted in worsening HF. The Adverse Event Advisory Committee further determined whether the HF events were associated with signs and/or symptoms of pulmonary congestion. The primary end point was the number of HF hospitalizations with pulmonary congestion, and the secondary end point was the number of HF health care utilization (HCU) events, defined as unscheduled office visits, urgent care visits, emergency department visits, or hospitalization, with pulmonary congestion. The committee members were blinded to the patients' HF device diagnostic parameters.

Combined HF device diagnostic algorithm development. In addition to providing CRT and ICD therapy, the devices used in this study had the capability to continuously monitor, record, and display various HF device diagnostic parameters referred to as the Cardiac Compass diagnostic report (10). The individual algorithms described in Table 1 were specified before the PARTNERS HF analysis and have been used to flag significant observations from the trends in Medtronic ICDs and CRT-Ds that were introduced in 2003 and 2004 or based on previous analyses. A low activity threshold (<1 h of activity per day) was fixed for all patients and was based on a

Table 1 Cardiac Compass HF Device Diagnostic Parameters and Algorithms

HF Device Diagnostic Parameter	Description	Algorithm
AF duration	The AF duration trend records the total time spent in AF on a daily basis; the detection algorithm for AF has been proven to be highly accurate (11).	AF ≥6 h on at least 1 day in patients without persistent AF (7 consecutive days with ≥23 h AF)
Ventricular rate during AF	This trend computes the daily average ventricular rate occurring during AF on that day (12).	AF = 24 h *and* the average ventricular rate during AF ≥90 beats/min on at least 1 day
Fluid index (OptiVol)	The fluid index corresponds to changes in thoracic fluid levels. The fluid index trend is the cumulative difference between the daily average and patient-specific reference intrathoracic impedances. The intrathoracic impedance is calculated from the voltage measured from an asynchronous current applied between the right ventricular lead and the device case (8,9).	High fluid index on at least 1 day; thresholds included ≥60, ≥80, and ≥100
Patient activity	This trend measures the total time active per day using a capacitive accelerometer. A minute is considered active if the counts exceed a threshold equal to walking approximately 70 steps/min (7).	Average patient activity <1 h over 1 week (nonoverlapping weekly windows)
Night heart rate	This trend measures the average ventricular rate from 12 AM (midnight) to 4 AM (7).	Average night heart rate >85 beats/min for 7 consecutive days (nonoverlapping weekly windows)
HRV	The median atrial heart rate is determined every 5 min, and a variability value is computed each day. HRV is not computed if >80% of the time is atrial pacing or AT/AF (7).	HRV <60 ms everyday for 1 week (minimum 5 measured days) (nonoverlapping weekly windows)
% of pacing CRT	This trend records the percentage of ventricular pacing on each day (13).	Ventricular pacing <90% for 5 of 7 days (nonoverlapping weekly windows)
ICD shock for potentially lethal VT/VF	This trend records whether a patient has received an automatic ICD shock for an episode detected as VT/VF and includes both appropriate and inappropriate shocks (14).	≥1 shocks during the evaluation period

AF = atrial fibrillation; AT/AF = atrial tachycardia/atrial fibrillation; CRT = cardiac resynchronization therapy; HF = heart failure; HRV = heart rate variability; ICD = implantable cardioverter-defibrillator; VT/VF = ventricular tachycardia/ventricular fibrillation.

previous analysis that led to this threshold being used in Medtronic released ICDs/CRT-D.

To determine the appropriate combined HF device diagnostic threshold criteria for identifying prospective risk of worsening HF, an independent internal development dataset (n = 819 patients) from a separate clinical registry trial (NCT00277524) was evaluated to determine the optimal number of these individual criteria that needs to be met to trigger the combined HF device diagnostic algorithm. We targeted having the algorithm trigger in less than a quartile of evaluations to maintain specificity. We determined that requiring only 1 criterion to be met would trigger the algorithm too often (43% evaluations), requiring 3 criteria would trigger too infrequently (3% evaluations), whereas requiring 2 criteria (14%) most closely matched our predetermined goal. Based on that analysis and previously published data on the specificity of the intrathoracic impedance fluid index, the final prospectively identified criteria included a fluid index >100 Ω days (9) or any 2 of the following criteria met during 1 evaluation period: long atrial fibrillation (AF) duration, rapid ventricular rate during AF, a high (≥60) fluid index, low patient activity, high night heart rate, low heart rate variability, low CRT pacing, or ICD shocks.

HF device diagnostic data from the first 60 days after implantation or enrollment were censored to establish the reference impedance. Patients with <5 months of follow-up or without the intrathoracic impedance HF device diagnostics were excluded from the analysis.

Statistical analysis. To evaluate the temporal dependency of the detection criteria, retrospective evaluations for the primary analysis were simulated every 15 days (semi-monthly), every 30 days (monthly), and also every 90 days (quarterly). Each simulation included: 1) a retrospective HF device diagnostic evaluation period to assess the patient's HF risk based on the HF device diagnostic trends; and 2) a prospective risk evaluation period to observe the first HF event occurrence (Fig. 1). Both the retrospective evaluation

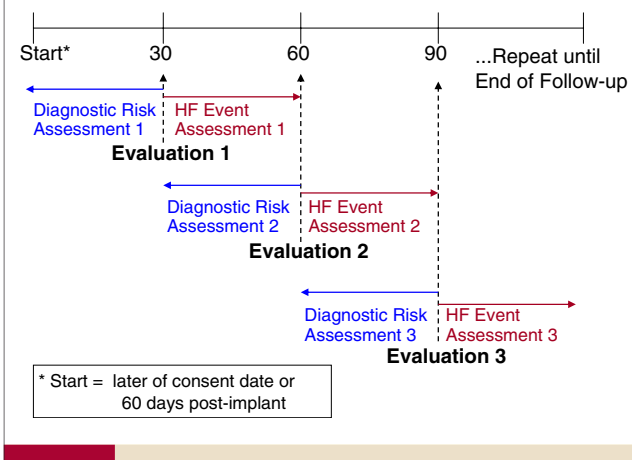

Figure 1 Monthly Review Model

Every 30 days the previous 30 days are evaluated for heart failure (HF) device diagnostic risk and then the subsequent 30 days are evaluated for HF event risk.

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and the prospective risk prediction periods were equal to the evaluation interval.

Continuous variables were presented as means and SDs, and categorical variables were presented as frequencies and percentages. We used Student *t* tests to compare continuous variables and chi-square tests for categorical variables.

Cox proportional hazards models (15) were used to determine the association between patients satisfying the HF device diagnostic criteria during the evaluation period and experiencing an HF event during the prospective evaluation period and to estimate the hazard ratios (HRs) and the 95% confidence intervals (CIs) of an HF event in a subsequent prediction period. For the monthly retrospective evaluation, each patient could have as many as 9 evaluation periods. To account for the correlation among evaluation periods within a patient, the robust sandwich variance estimate (16) for the HR was applied. Cox regression models were used for adjusting several clinical variables, including age, sex, ischemic cardiomyopathy, diabetes, NYHA functional class, and use of beta-blockers, diuretics, or angiotensin-converting enzyme inhibitors/angiotensin receptor blockers.

We also conducted a subgroup analysis to establish the predictive power of the HF device diagnostics within the 2 following subgroups: 1) patients without a previous HF event; and 2) patients with a previous HF event. We performed the subgroup analysis by dividing patients' evaluations into 2 groups: those with and without HF events in the previous evaluation periods. In patients with an HF event, all evaluation periods for that patient were considered to be in the HF group after the initial event.

All statistical tests were conducted at a significance level of 0.05, and all statistical analyses were performed using SAS software (version 9.1, SAS Institute Inc., Cary, North Carolina).

Results

Patient demographics and events. A total of 1,024 patients were enrolled at 100 centers in the United States. The present analysis included all 694 patients who had Medtronic CRT-D with a fluid index-monitoring capability. All patients were followed for at least 5 months, with an average follow-up of 11.7 ± 2.0 months. Patient demographic and medication information is shown in Table 2. Patients in this study were typical of a CRT-D patient population: the majority had an ischemic cardiomyopathy, 95% had an NYHA functional class III HF status at the beginning of the study, and one-fourth of the patients had a history of AF. Most patients were receiving angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (81%) as well as beta-blockers (89%) and diuretics (83%).

Ninety (13%) patients had 141 adjudicated HF hospitalizations with pulmonary congestion. The overall event rate for the individual evaluation periods was very low due to the high number of evaluations, especially for semimonthly and monthly periods. The percentages of evaluations with a pulmonary HF hospitalization were as follows: monthly, 1.4% (78 events/5,693 evaluations); quarterly, 3.2% (60 HF events/1,854 evaluations); and semimonthly, 0.76% (87 events/11,452 evaluations). In the 120 (17.3%) patients who had at least 1 HCU, the total number of HCUs with pulmonary congestion was 213. These 213 HCUs included the 141 HF hospitalizations as well as 51 unscheduled office visits, 5 urgent care visits, and 100 emergency department visits. Of 694 patients, 15 (2.2%) died.

Combined algorithm performance. The combined algorithm triggered criteria in 23% (1,324 of 5,693) of the evaluations and in 43% (298 of 694) of the patients. Figure 2 shows a breakdown of which individual parameters were triggered. Two or more of the 8 criteria were triggered in

Table 2 Baseline Patient Characteristics (n = 694)

Age (yrs)	68.4 (10.7)
Males	67.3
Ethnic origin	
African American	10.7
Caucasian	85.3
Hispanic	0.7
Native American	0.6
Other or no information	2.9
% patients with LVEF ≤35%	99.1
% patients with QRS duration ≥130 min	99.3
Heart failure etiology	
Ischemic	62.2
Nonischemic	37.8
Diabetes (type 1 or 2)	42.4
Respiratory	57.5
COPD	19.2
Atrial fibrillation	25.8
Chronic/permanent	1.2
Persistent	3.2
Paroxysmal	22.0
New York Heart Association functional class	
III	94.8
IV	5.2
ACC/AHA heart failure stage	
C	98.3
D	1.7
Cardiovascular medications	
Anticoagulants/antiplatelets	84.1
ACE inhibitors or ARBs	82.6
Beta-blockers	90.6
Antiarrhythmics (class I/III)	16.9
Cardiac glycosides	34.7
Diuretics	83.6
Vasodilators/nitrates	29.8
Lipid-lowering medications	69.2

Values are mean (SD) or %.

ACC/AHA = American College of Cardiology/American Heart Association; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction.

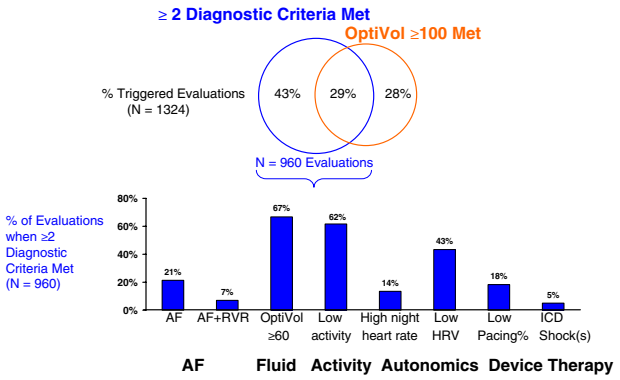

Figure 2 Combined HF Device Diagnostics Triggered

The Venn diagram shows that 72% of evaluations had ≥2 HF device diagnostics triggered with the remaining 28% triggered by OptiVol Fluid Index ≥100. OptiVol Fluid Index, low activity, and low heart rate variability (HRV) were the most common reasons for triggers. AF = atrial fibrillation; ICD = implantable cardioverter-defibrillator; RVR = rapid ventricular response; other abbreviation as in Figure 1.

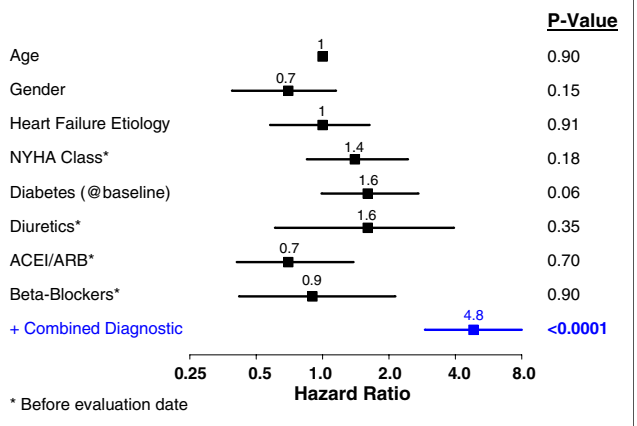

Figure 4 Multivariable Analysis

Patients with a positive combined HF device diagnostic had a 4.8-fold increased risk of an HF event within 30 days after adjusting for clinical variables. ACEI/ARB = angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; NYHA = New York Heart Association; other abbreviation as in Figure 1.

72% of the algorithm triggers, whereas a fluid index of ≥100 alone was triggered in an additional 28%. In the 954 evaluations with ≥2 criteria triggered, a high fluid index, low activity, and low heart rate variability were the most common criteria met, followed by long AF duration, low CRT pacing, high night heart rate, rapid ventricular rate during AF, and ICD shocks. Three criteria were triggered in 20% of the evaluations and 4 or 5 in the remaining 8%.

Figure 3 shows the Kaplan-Meier survival curve for monthly evaluations. Compared with patients with a negative combined HF device diagnostic, patients with a positive combined HF device diagnostic had a significantly increased risk of an HF hospitalization with pulmonary congestion within the next month (HR: 5.5, 95% CI: 3.4 to 8.8), $p < 0.0001$). The combined algorithm was also good at identifying which patients were at low risk of subsequent HF events as only 0.7% of patients with a negative HF device diagnostic had an HF hospitalization during the subsequent 30 days. After adjusting for clinical variables known to affect the occurrence of HF events (Fig. 4), patients with a positive combined HF device diagnostic had a 4.8-fold increased risk (HR: 4.8, 95% CI: 2.9 to 8.1, $p < 0.0001$) of a subsequent HF hospitalization with pulmonary congestion independent of the other clinical variables. None of the other predefined clinical variables significantly identified patients at a higher risk of an HF event.

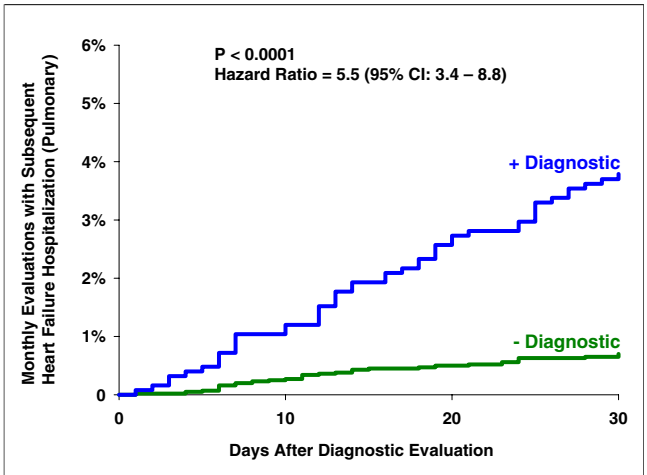

Figure 3 Kaplan-Meier Estimates of the Percentage of Monthly Evaluations With a Subsequent HF Hospitalization Due to Sign/Symptoms of Pulmonary Congestion

Patients with a positive combined HF device diagnostic algorithm had a 5.5-fold increased risk of a subsequent HF event within 30 days. CI = confidence interval; other abbreviation as in Figure 1.

Other analyses. In addition to the combined algorithm performance, we analyzed the performance of various components of the combined algorithm (Fig. 5A). Increasing the fluid index thresholds resulted in higher HRs. A low (≥60) fluid index threshold identified patients at a 2.7-fold risk of HF hospitalization with pulmonary congestion; however, a high (≥100) fluid index increased the HR to 3.9 ($p < 0.0001$ for both). The HR (3.2) for 1 of the 7 HF device diagnostic criteria met (excluding fluid index) was similar to the HR (3.3) for a fluid index ≥80. Requiring any 2 of the 7 HF device diagnostic criteria (excluding fluid index) increased the HR dramatically but resulted in a smaller subset of patients meeting that condition.

A subanalysis to determine the algorithm performance in patients with as opposed to without a previous HF event during the simulated evaluations revealed 63 evaluations with HF hospitalizations in which the patient did not have

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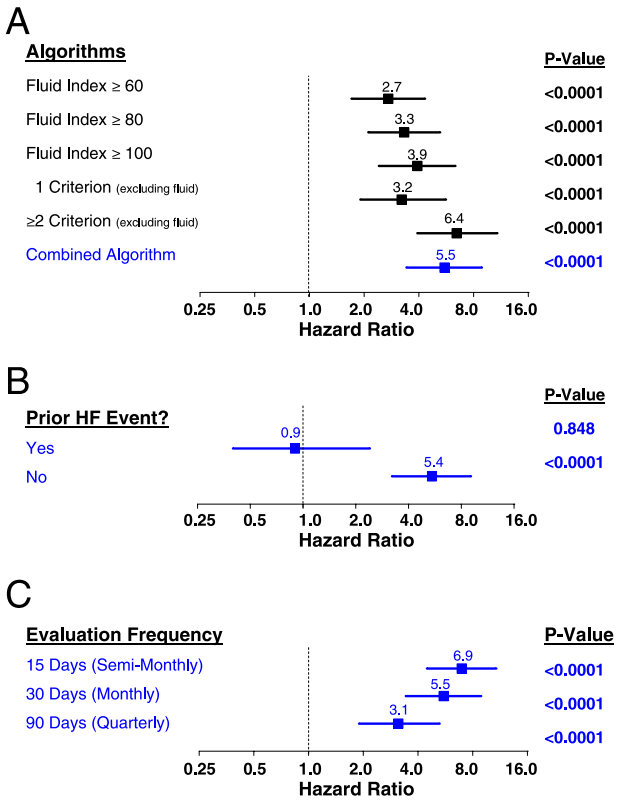

Figure 5 **Risk Stratification for Different Algorithms, HF Event History, and Evaluation Frequencies**

(A) Various algorithms. An increasingly higher fluid index threshold identifies patients at higher risk as does combined HF device diagnostic algorithms. **(B)** History of HF event. In patients without a previous HF event, the combined HF device diagnostic did not identify patients at high risk of a subsequent event; however, in patients without a previous event, the combined HF device diagnostic algorithm identified patients at a 5.4-fold increased risk of a subsequent HF event within 30 days. **(C)** Evaluation frequency. Increasing the frequency of reviewing the HF device diagnostics from quarterly to monthly will substantially increase the ability to identify patients at higher risk, whereas changing from monthly to semimonthly provides a less notable increase. Abbreviation as in Figure 1.

a previous HF hospitalization during the study. For these patients, the combined algorithm identified patients who had a 5.4-fold increased risk (HR: 5.4, 95% CI: 3.2 to 9.0, $p < 0.0001$) of HF hospitalization within the following month, as shown in Figure 5. The HR remained high after adjusting for the clinical variables (HR: 4.7, 95% CI: 2.8 to 8.0, $p < 0.0001$). There were 15 evaluations with an HF hospitalization in patients who already had an event earlier in the study. The combined HF device diagnostic algorithm did not provide risk stratification in those patients with a previous event (HR: 0.9, 95% CI: 0.3 to 2.4, $p = 0.8$).

We further sought to understand the effect of less frequent evaluations (quarterly: every 90 days) and more frequent evaluations (semimonthly: every 15 days). The risk-stratification capability of the combined HF device diagnostic algorithm dropped when we moved from semi-monthly evaluation to monthly evaluation, and there was a further drop when done at quarterly evaluations (semi-monthly HR of 6.9 vs. monthly HR of 5.5 vs. quarterly HR of 3.1), as shown in Figure 5C.

Discussion

The PARTNERS HF study is the largest prospective cohort study evaluating the ability of combined HF device diagnostics to dynamically risk-stratify patients for HF events over set time intervals. Device diagnostic data were independent predictors of HF hospitalizations with pulmonary symptoms. More frequent evaluation of HF device diagnostics improved the ability to risk-stratify patients for subsequent HF events.

In the current study, the use of multiple parameters significantly improved the ability to identify patients at risk of HF events in the subsequent 30 days beyond the use of intrathoracic impedance alone (combined HF device diagnostic HR of 5.5 vs. fluid index ≥60 HR of 2.7). Previous studies focused on intrathoracic impedance monitoring to predict future events without looking at other diagnostic parameters or they have looked at single HF device diagnostic parameters without combining them into an algorithm. The relationship between intrathoracic impedance and changes in fluid status has been proven by some studies that showed a significant correlation between impedance measurements and N-terminal pro–B-type natriuretic peptide concentration and pulmonary capillary wedge pressure (17). Relating changes in impedance to HF symptoms and clinical events has been more difficult. Ypenburg et al. (9) found that only 33% of the patients (n = 15) in their study with an OptiVol alert set at 60 Ω had HF symptoms. Likewise, other studies have looked at other HF device diagnostics such as night heart rate, heart rate variability, and activity but have not coupled them with intrathoracic impedance monitoring (7).

Another important finding of our study is that increasing the frequency of evaluation from quarterly evaluations improves the ability of the combined HF device diagnostic data to predict subsequent HF events in the near term. It is unclear whether this improved ability to risk-stratify patients will translate into improved outcomes. In past studies of HF disease management evaluating interventions that included daily measurement of physiologic parameters (weight, blood pressure, or heart rate) and/or responses to questions, these parameters taken together have shown a mixed impact on hospital admission rates. Investigators in the SPAN CHF II (Specialized Primary and Networked Care in Heart Failure) study evaluated a home monitoring system providing daily measurements of blood pressure and weight with patient survey results. These measurements improved the 90-day outcomes for HF hospitalization (0.51 vs. 1.82 per patient-year, $p = 0.03$) (18). In the Trans-

European Network Homecare Monitoring Study, the number of all-cause and HF admissions was higher in the daily telemonitoring cohort compared with usual care (155 vs. 69 for all-cause; 67 vs. 33 for HF hospitalization; no p values provided). In the Weight Monitoring in Heart Failure study, twice-daily monitoring had no impact on cardiovascular rehospitalizations (0.11 ± 0.26 vs. 0.08 ± 0.24, p = 0.28) (19). These patients were enrolled at the time of discharge from the hospital. In the current study, once patients experienced an HF hospitalization, the ability of HF device diagnostic data to stratify them by risk was absent, but no definite conclusions could be drawn regarding this observation due to the small number of events. In the patients without a previous HF event, the patients with a positive combined HF device diagnostic were 5.4 times more likely to have a subsequent event, which suggests the HF device diagnostics can help stratify patients at higher risk in this important set of patients.

Physicians can now receive reimbursement for remote monitoring if the HF device diagnostic data are reviewed every 30 days or less often. The PARTNERS HF investigators identified a large improvement in risk stratification when they reduced the duration between evaluations from 90 days to 30 days, but they observed a smaller improvement in risk stratification when the duration decreased from 30 days to 15 days. These results suggest that 30 days may be the optimal time frame for review of HF device diagnostics.

Study limitations. The present results may be specific to the device models studied and may not necessarily be extrapolated to other devices with different combinations of parameters because the specific combinations of device-derived patient HF device diagnostics can vary between models and between manufacturers. Because the PARTNERS HF study was based on an unblinded prospective registry of HF patients with reduced left ventricular function who had received appropriate implantable devices, the ability of HF device diagnostics to risk-stratify a broader HF population can only be inferred from our results. In addition, because clinicians were not blinded to HF device diagnostic trends, they may have acted on these trends and changed the natural course of the disease to avoid a clinical event. This type of action would lead to underestimation of the HF device diagnostic data's predictive performance. Likewise, a patient being seen for abnormal HF device diagnostics for which an HF event was then reported would result in an overestimation of the algorithm performance. However, this scenario was unlikely to occur because the Adverse Event Advisory Committee adjudicated reported events as "no HF event" if the HF device diagnostics were indicated as the cause of the event when no other signs or symptoms of HF were present. The limited number of events warrants replication in a follow-up analysis to verify our results.

Conclusions

Changes in HF device diagnostic parameters based on a combined algorithm can stratify HF patients for subsequent HF events into high and low risk. The lack of positive HF device diagnostic criteria during a 30-day evaluation period identified a cohort of patients who were at very low risk of subsequent HF clinical events. In contrast, a positive HF device diagnostic criterion identified patients who were 4.8 times more likely to experience an HF hospitalization with pulmonary congestion in the next 30 days. Although not all patients subsequently experienced an HF hospitalization with pulmonary congestion, the finding that these patients are at an increased risk of HF events suggests that these patients have become unstable and should be viewed as high risk. This study was not a randomized trial to determine whether clinical interventions based on the HF device diagnostics will improve outcomes. Future studies are needed to test that hypothesis.

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