ORIGINAL ARTICLE

Prospective Study

Comparison of partners-heart failure algorithm *vs* care alert in remote heart failure management

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Abstract

AIM: To compare the utility of the partners-heart failure (HF) algorithm with the care alert strategy for remote monitoring, in guiding clinical actions oriented to treat impending HF.

METHODS: Consecutive cardiac resynchronization-defibrillator recipients were followed with biweekly automatic transmissions. After every transmission, patients received a phone contact in order to check their health status, eventually followed by clinical actions, classified as "no-action", "non-active" and "active". Active clinical actions were oriented to treat impending HF. The sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of the partners-HF algorithm *vs* care alert in determining active clinical actions oriented to treat pre-HF status

and to prevent an acute decompensation, were also calculated.

RESULTS: The study population included 70 patients with moderate to advanced systolic HF and QRS duration longer than 120 ms. During a mean follow-up of 8 ± 2 mo, 665 transmissions were collected. No deaths or HF hospitalizations occurred. The sensitivity and specificity of the partners-HF algorithm for active clinical actions oriented to treat impending HF were 96.9% (95%CI: 0.96-0.98) and 92.5% (95%CI: 0.90-0.94) respectively. The positive and negative predictive values were 84.6% (95%CI: 0.82-0.87) and 98.6% (95%CI: 0.98-0.99) respectively. The partners-HF algorithm had an accuracy of 93.8% (95%CI: 0.92-0.96) in determining active clinical actions. With regard to active clinical actions, care alert had a sensitivity and specificity of 11.05% (95%CI: 0.09-0.13) and 93.6% respectively (95%CI: 0.92-0.95). The positive predictive value was 42.3% (95%CI: 0.38-0.46); the negative predictive value was 71.1% (95%CI: 0.68-0.74). Care alert had an accuracy of 68.9% (95%CI: 0.65-0.72) in determining active clinical actions.

CONCLUSION: The partners-HF algorithm proved higher accuracy and sensitivity than care alert in determining active clinical actions oriented to treat impending HF. Future studies in larger populations should evaluate partners-HF ability to improve HF-related clinical outcomes.

Key words: Heart failure; Cardiac resynchronization therapy; Defibrillators; Remote monitoring

Core tip: This is a multicenter observational registry that compared the utility of the partners-heart failure (HF) algorithm with the care alert strategy for remote monitoring, in guiding clinical actions oriented to treat impending HF in a population of 70 cardiac resynchronization therapy recipients followed over a mean follow-up period of 8 ± 2 mo. The partners-HF algorithm displayed high sensitivity (96.9%), specificity (92.5%), positive (84.6%) and negative (98.6%) predictive values for active clinical actions oriented to treat impending HF. The care alert exhibited lower sensitivity (11.1%), positive (42.3%) and negative (71.1%) predictive values.

INTRODUCTION

Heart failure (HF) is a primary public health problem, with mortality and hospitalization rates of approximately 7.2% and 31.9% at one-year respectively[1]. Outpatient management, symptoms and daily weight often do not identify patients in time to prevent imminent HF. Modern implantable cardiac resynchronization therapy-defibrillators (CRT-D) with remote monitoring (RM) capabilities, continuously assess parameters, including heart rate, patient's activity (PA), intra-thoracic impedance, atrial fibrillation (AF), ventricular arrhythmias (VA), shock therapy delivered and system integrity[2-5].

Previous studies have demonstrated the ability of individual device diagnostic data, to predict HF events, to reduce the time from clinical event to treatment, length of hospitalization and quantity of in-office visits[6-10].

Earlier studies have shown that implantable device-measured parameters, such as intra-thoracic impedance, AF burden, mean heart rate, heart rate variability (HRV), patient activity (PA), frequency of premature ventricular contractions (PVCs), VA episodes, implantable cardioverter defibrillators (ICD) shocks and percentage of pacing of cardiac resynchronization therapy (%CRT), individuate subjects at risk of HF and facilitate early interventions[6-12]. Variations of intrathoracic impedance[3] as well as HRV and PA[2] occurs nearly two weeks before HF exacerbation. Low HRV indicate a sympathetic dominance in cardiac autonomic control and may be associated with exacerbation of atrial and VAs[13]. A prolonged AF duration, a rapid ventricular rate (VR) during AF and an increase in the burden of PVCs reduce %CRT[14] and are warning signs of HF, together with ICD shocks[15].

Each HF device diagnostic parameter, although validated in various studies, has several limitations. A previous study[16] showed that sensitivity values of individual parameters, ranged from 23.6% to 50.0%, whereas their combination displayed 65.4% sensitivity and 99.5% specificity for cardiovascular hospitalizations and deaths.

The partners-HF[11] is the largest cohort study to have evaluated the ability of combined HF device diagnostics, including Optivol™ Fluid index, AF duration, rapid VR during AF, low PA, high nocturnal heart rate (NHR), low HRV, low CRT pacing percentage, and ICD shocks, to identify patients at risk of acute HF in the subsequent 30 d. The retrospective analysis of the prospectively collected data of the partners-HF study, demonstrated that subjects with a positive partners-HF algorithm were at a greater risk (HR = 5.5; $P < 0.001$) of HF hospitalization during the next month.

The purpose of this multicenter, observational registry was to prospectively assess the utility of the partners-HF criteria, implemented within Discovery Link™, in guiding clinical actions oriented to treat pre-HF status and to prevent an acute decompensation in a population of HF individuals implanted with a Medtronic CRT-D device.

MATERIALS AND METHODS

Registry population and design

This study has been approved by our Institutional Review Board and is conform to the guiding principles of the Declaration of Helsinki.

Consecutive CRT-D candidates were enrolled by three Italian cardiology centers. The clinical status of the patients, including NYHA class, was initially assessed by the cardiologists involved in the project. All patients underwent implantation of a Medtronic CRT-D system (Model: Consulta™, Concerto™ Ⅱ, VIVA XT™, PROTECTA XT™; Medtronic Inc., Minnesota) equipped with the CareLink Medtronic®-RM system for RM.

Inclusion criteria were: Left ventricular ejection fraction ≤ 35% + NYHA class Ⅱ, Ⅲ and ambulatory Ⅳ and broad QRS (> 120 ms if left bundle branch block was present, or otherwise > 150 ms + optimal pharmacological treatment for HF). Exclusion criteria were: acute coronary syndrome within 40 d, coronary artery revascularization within 3 mo, end-stage HF requiring inotropic support, ventricular assist devices or dialysis.

Each patient received a wireless CareLink Monitor which provided automatic transmission of clinical and technical parameters stored in the implanted device's memory to a Service Center where information was decrypted, uploaded to a secure website and periodically accessed by the nurses. Patients were followed up for at least 6 mo. Data were prospectively collected between January 2012 and October 2012 and classified on the basis of both the care alert and the partners-HF algorithms at the same time. Automatic "scheduled" transmissions were programmed every 15 d. "Care alert"-triggered transmissions and transmissions activated manually by the patients were also collected. Patients were instructed to manually activate transmissions in case of occurrence or exacerbation of HF-related symptoms (including shortness of breath, dyspnea, orthopnea, asthenia, pre-syncope or syncope) or signs (including weight increase, peripheral edema enlargement).

The project, including data collection, was approved by the Hospital Ethics Committees of each cardiology center involved in the registry using the Medtronic Clinical Service Project®, and every individual enrolled gave written informed consent to enrolment in the registry.

Partners-HF algorithm

The partners-HF application, based on the algorithm described by Whellan *et al*[11], was implemented within the Discovery Link™. The latter is a web environment enabling elaborated and aggregated information from the Medtronic CareLink Network® to be shown in interactive JavaScript charts. The partners-HF algorithm was adopted to process information in order to select the last transmission (including both manually and automatically triggered ones) from each device and to perform analysis. Statistics were calculated over the last 28 consecutive days[11]. Every two weeks, the first partners-HF profile of those patients who satisfied the partners-HF criteria was directly logged into the Discovery Link.

The partners-HF algorithm was considered positive in the following cases: Optivol™ Fluid index ≥ 100 or any 2 of the following criteria met during a one-month period of evaluation: Long AF duration, rapid VR during AF, Optivol™ fluid index ≥ 60, low PA, high nocturnal NHR, low HRV, low %CRT, and ICD shocks (Appendix).

Care alert

The Carelink system automatically triggered alerts in case of shocks delivered or if the following clinical and technical parameters exceed a programmable threshold: OptiVol™ Fluid Monitoring Index (> 60), AF duration (> 24 h), VR rate during AF (> 100 bpm), lead impedance, integrity and battery voltage alert (out of predefined range).

Adjudication of impending heart failure and classification of clinical actions

After every transmission, all patients received a phone contact and their health status was checked by nurses experienced in HF. At time of enrollment, patients were instructed to measure frequently their body weight and to check their pulse in order to identify HF-related signs (increase of heart rate, weight and/or peripheral edema) and symptoms (increase in shortness of breath, cough and/or asthenia, reduction of exercise tolerance, needing use of extra pillows during the night). Data on vital status, symptoms, quality of life, adherence to pharmacological treatment, hospitalizations and mortality were collected by nurses at every phone contact. Pre-specified boundaries for weight, blood pressure, pulse and symptoms were previously established for every patient. Adjudication of impending HF was based on the development of early HF-related signs and symptoms (see above) and on the exceeding from the prespecified boundaries, but still not requiring hospitalization[12]. RM transmissions suggestive of worsening HF or device malfunctioning were submitted to physicians.

Clinical actions performed as a result of transmissions, according to each center's clinical practice, were registered on a Medtronic Clinical Service®-form and were classified as follows: "no-action", "non-active" and "active". No action: (1) consisted on telephonic contact; (2) non-active clinical action; (3) consisted on clinical examination without pharmacological treatment modification (PTM). Active clinical actions included PTM during telephonic contact; or (4) during clinical examination. In the event of manual or care alert transmissions, physicians could decide either to undertake clinical action immediately or to wait until the first partners-HF data from those specific transmissions

Table 1 Study population

Clinical characteristics of the study population	
Age (yr)	70.3 ± 8.3
Male (%)	78.3
EF (%)	27.5 ± 6.5
Etiology post-ischemic DC (%)	63.2
Idiopathic DC (%)	33.7
Valvular DC (%)	2
Congenital DC (%)	1.1
NYHA Ⅱ (%)	17.3
Ⅲ (%)	78.6
Ⅳ (%)	4.1
Optimized pharmacological treatment (%)	63.2[1]
Prevention: Primary (%)	73.7
Secondary (%)	18.3
SVT (%)	3.7
Syncope (%)	3.2
Cardiac arrest (%)	5.1
AF permanent (%)	16.3
Persistent (%)	7.4
Paroxysmal (%)	4.1
Devices: Consulta™ CRT-D	37.4
Concerto™ Ⅱ CRT-D (%)	26.3
Viva XT™ CRT-D (%)	22.1
Protecta XT™ CRT-D (%)	14.2

[1]The low percentage of optimized pharmacological treatment is related to reduce aldosterone antagonists administration in patients affected by chronic kidney disease. EF: Ejection fraction; DC: Dilated cardiomyopathy; NYHA: New York Heart Association; SVT: Sustained ventricular tachycardia; AF: Atrial fibrillation; CRT-D: Cardiac resynchronization therapy-defibrillator.

became available in the Discovery Link environment.

Study endpoints
The aim of this study was to determine the sensitivity, specificity, positive and negative predictive values and diagnostic accuracy of the partners-HF algorithm and of care alert in determining active clinical actions oriented to treat pre-HF status and to prevent an acute decompensation. Analyses of sensitivity, specificity, predictivity and accuracy were performed with respect to overall active clinical actions (3 + 2) *vs* the sum of clinical actions and no actions (1 + 0).

Statistical analysis
Continuous variables are summarized as mean ± SD and categorical variables as counts and percentages. Positive transmissions by the partners-HF algorithm and/or care alert were considered true positive when they were associated with acute HF and/or with pharmacological treatment modification due to impending HF. Positive transmissions by the partners-HF algorithm and/or care alert were considered as false positive in the remaining cases. Negative transmissions by the partners-HF algorithm and/or care alert were considered true negative when they were not associated to acute HF or PTM due to pre-HF (see above), and as false negative when they were not. The sensitivity of the partners-HF algorithm and of care alert was calculated as the ratio between the number of true positive
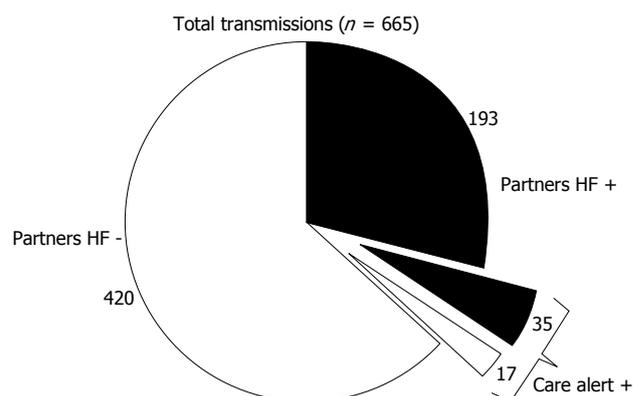

Figure 1 Distribution of total transmissions. Legend total transmissions are depicted in a pie-chart; positive partners-HF transmissions are shown in black; negative partners-HF transmissions are shown in white. Care alert transmissions are represented in separate slices. HF: Heart failure.

transmissions and the sum of true positive and false negative transmissions. Specificity was calculated as the ratio between true negatives and the sum of true negatives and false positives. Positive predictive value was calculated as the ratio between true positives and the sum of true positives and false positives. Negative predictive value was calculated as the ratio between true negatives and the sum of true negatives and false negatives. Accuracy was calculated as the ratio between the sum of true positive and true negative transmissions and total transmissions. All the tests were performed by means of R 2.11.1 for Windows.

RESULTS

Study population
The characteristics of the study population are presented in Table 1. Patients were predominantly males and had mostly a moderate to advanced HF. All patients had QRS duration longer than 120 ms. The relatively low (63.2) percentage of optimized pharmacological treatment is due to reduced aldosterone antagonists administration in patients affected by chronic kidney disease.

Transmissions
During a mean follow-up of 8 ± 2 mo, 665 transmissions were received from 70 patients. Transmissions were classified as follows: 52 (7.8%) care alert, 149 (22.4%) manual and 464 (69.8%) scheduled.

Of all transmissions, 228 (34.3%) fulfilled the partners-HF criteria. Positive partners-HF transmissions were classified as: scheduled (136; 59.6%), manual (57; 25%), and care alert (35; 15.4%). Of the 437 negative partners-HF transmissions, 328 (75.1%) were scheduled, 92 (21%) were manual and 17 (3.9%) were triggered by a care alert. Figure 1 shows the distribution of partners-HF positive and negative transmissions, contemporarily triggered or not by care alert. Overall, the "care alert" transmissions met the partners-HF criteria in 67.3% of cases (Figure 1).
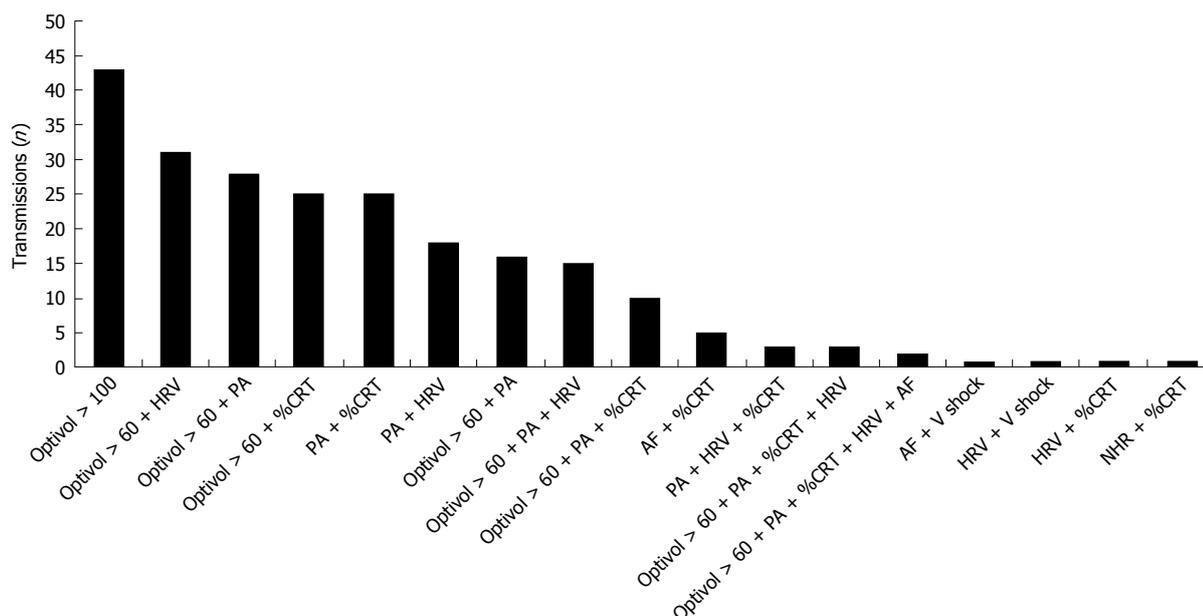
Figure 2 Positive partners-heart failure transmissions. HRV: Heart rate variability; PA: Patient activity; %CRT: Percentage of cardiac resynchronization therapy pacing; AF: Atrial fibrillation; V shock: Ventricular shock; NHR: Night heart rate.

Table 2 Pharmacological treatment modifications following positive or negative partners-heart failure transmissions and care alert

Active clinical actions	Partners-HF +	Care alert +
Pharmacological treatment modification during telephonic contact		
Diuretic dosage increase	120	25
BB dosage increase	57	22
AAD administration	2	2
ACE-I and ARA dosage increase	4	0
OAC administration	5	5
Clinical examination and pharmacological treatment modification		
Diuretic dosage increase	9	4
BB dosage increase	8	3
AAD administration	1	1
ACE-I and ARA dosage increase	1	1
Anti-platelet administration	0	0

+: Positive; BB: Beta-blockers; AAD: Anti-arrhythmic drugs; ACE-I: Angiotensin-converting-enzyme inhibitors; ARA: Angiotensin II-receptor antagonists; OAC: Oral anti-coagulant; HF: Heart failure.

The most common reasons triggering a positive partners-HF transmission: Optivol fluid index ⩾ 100 (18.8%) or optivol fluid index > 60 plus one of the following parameters: reduced HRV (13.6%), low PA (12.3%), or reduced %CRT (11%) (Figure 2). The 52 "care alert"-triggered transmissions (35 partners-HF positive and 17 partners-HF negative) were generated by OptiVol fluid index in 43 (82.7%) cases, AF duration and/or AF VR in 7 (13.5%) cases and shock for VAs in 2 (3.8%) cases.

Clinical actions following transmissions

During follow-up, no deaths or HF hospitalizations occurred. Of overall transmissions, 16 (2.4%) were followed by clinical examination and PTM, 183 (27.5%) by PTM during telephonic contact and 7 (1%) by clinical examination without PTM.

Of the 228 positive partners-HF transmissions, 11 (4.8%) were followed by clinical examination and PTM, 182 (79.8%) by PTM during telephonic contact and 6 (2.7%) by clinical examination without PTM (Figure 3A). PTM consisted of 19 drug dosage up-titrations and/or new treatment administrations during clinical examination and 188 during telephonic contact (Table 2). No pharmacological down titration was done.

Of the 437 negative partners-HF transmissions, 5 (1.1%) were followed by clinical examination and PTM, 1 (0.2%) by PTM during telephonic contact and 1 (0.2%) by clinical examination without PTM (Figure 3B). PTM consisted of 7 drug dosage up-titrations and/or new treatment administrations during clinical examination and 2 telephonic PTM, made as a consequence of a single care alert transmission. In these cases, diuretic and beta-blocker dosages were increased; no pharmacological down titration was reported.

Of the 52 care alert transmissions, 4 (7.7%) were followed by clinical examination and PTM and 18 (34.6%) by PTM during telephonic contact (Figure 3C). PTM consisted of 9 drug dosage up-titrations and/or new treatment administrations during clinical examination and 54 without in-office clinical examinations (Table 2).

Clinical actions following negative care alert transmissions consisted of 12 (1.9%) clinical examinations and PTM, 165 (27%) PTM during telephonic contact, 7 (1.1%) clinical examinations without PTM and 429 (70%) telephone contacts alone. PTM consisted of 17 drug dosage up-titrations and/or new treatment administrations during clinical examination and 136 without in-office clinical examinations.

Diagnostic accuracy of partners-HF and care alert

True positive, true negative, false positive and false

A

Partners-HF +

4.8%   12.7%

2.7%

79.8%

B

Partners-HF -

1.1%

0.2%

0.2%

98.5%

☐ No action 0
☐ Clinical action 1
▨ Active clinical action 2
■ Active clinical action 3

C

Care alert

7.7%

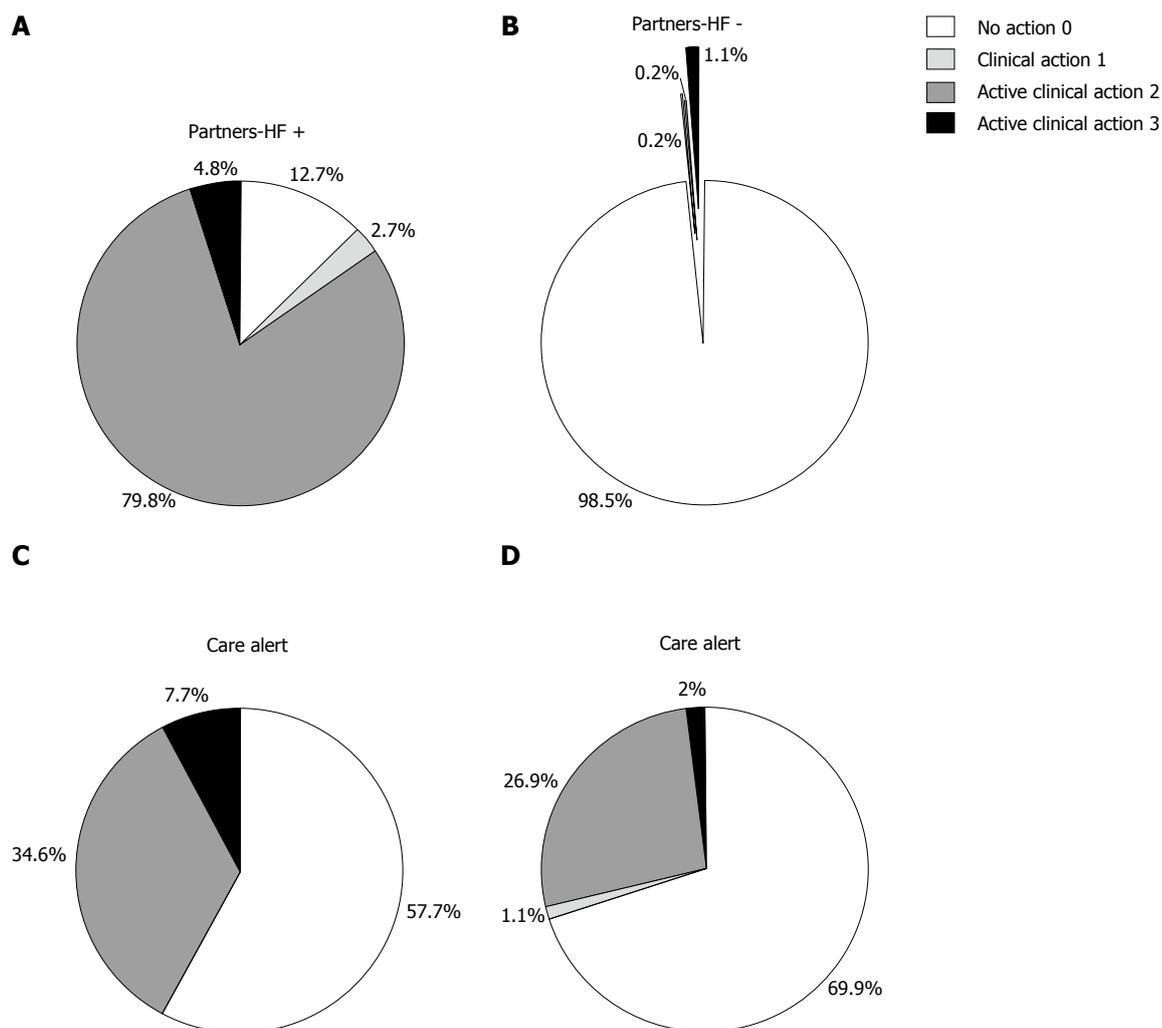34.6%

57.7%

D

Care alert

2%

26.9%

1.1%

69.9%

Figure 3 Clinical actions following positive partners-heart failure, negative partners-heart failure, positive care alert and negative care alert transmissions. No actions are depicted in white; clinical actions are depicted in light gray; active clinical actions are depicted in dark gray (pharmacological treatment modifications during telephonic contacts) and black (clinical examination and pharmacological treatment modifications). HF: Heart failure.

negative partners-HF transmissions with respect to active clinical actions are depicted in Figure 4A. The sensitivity and specificity of the partners-HF algorithm for active clinical actions (classes 2-3) were 96.9% (95%CI: 0.96-0.98) and 92.5% (95%CI: 0.90-0.94) respectively (Table 3). The positive and negative predictive values were 84.6% (95%CI: 0.82-0.87) and 98.6% (95%CI: 0.98-0.99) respectively. The partners-HF algorithm had an accuracy of 93.8% (95%CI: 0.92-0.96) in determining active clinical actions (Table 3).

Care alert true positive, true negative, false positive and false negative transmissions with respect to active clinical actions are depicted in Figure 4B. With regard to active clinical actions (classes 2-3), care alert had a sensitivity and specificity of 11.05% (95%CI: 0.09-0.13) and 93.6% respectively (95%CI: 0.92-0.95). The positive predictive value was 42.3% (95%CI: 0.38-0.46); the negative predictive value was 71.1% (95%CI: 0.68-0.74). Care alert had an accuracy of 68.9% (95%CI: 0.65-0.72) in determining active clinical actions

(Table 3).

DISCUSSION

Main findings

In this registry we observed that: (1) The partners-HF algorithm has high sensitivity (96.9%), specificity (92.5%) and diagnostic accuracy (93.8%) in identifying patients with early HF-related symptoms and signs (pre-HF), at risk of acute HF, who benefit from active clinical actions; (2) The care alert displays good specificity (93.5%) but very low sensitivity (11.1%) in identifying patients with pre-HF who benefit from active clinical actions; (3) Of all the CRT-D remote transmissions, 34.3% fulfilled the partners-HF criteria and 7.8% were triggered by a care alert. Positive partners-HF transmissions also determined a care alert in 15.4% of cases, and care alert transmissions met partners criteria in 67.3% of cases; (4) The most common reasons triggering a Positive partners-HF transmission were: Optivol fluid index $\geqslant$ 100 (18.8%) or optivol fluid index

Table 3 Diagnostic accuracy of partners-heart failure and care alert in determining active clinical actions

	Active clinical actions (2-3)	Non-active/no clinical actions (0-1)	Total transmissions
Positive partners-HF transmissions	193	35	228
Negative partners-HF transmissions	6	431	437
Positive care alert transmissions	22	30	52
Negative care alert transmissions	177	436	613
Overall transmissions followed by an action	199	466	665
Appendix partners-HF algorithm			
Parameters	Criterion		
Fluid index	$\geqslant$ 60 d		
AT/AF duration	$\geqslant$ 6 h and not persistent AT/AF		
VR during AT/AF	AT/AF $\geqslant$ 24 h and VR $\geqslant$ 90 bpm		
Patient activity	< 1 h over 1 wk		
NHR	$\geqslant$ 85 bpm for 7 consecutive days		
HRV	< 60 ms for 7 consecutive days		
%CRT pacing	< 90% for 5 of 7 d		
Shock (s)	$\geqslant$ 1 shock		

AT: Atrial tachycardia; AF: Atrial fibrillation; VR: Ventricular rate; NHR: Night heart rate; HRV: Heart rate variability; CRT: Cardiac resynchronization therapy; HF: Heart failure.
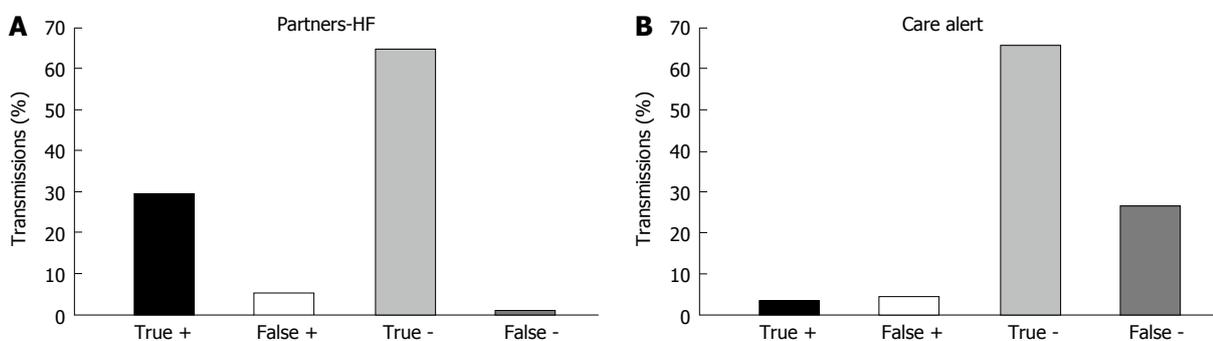

Figure 4 True and false positive and negative transmissions according to active clinical actions. A: True +: Positive partners-HF transmissions followed by active clinical actions (class 2 or 3); False +: Positive partners-HF transmissions followed by no actions or non-active clinical actions (class 0 or 1); True -: Negative partner-HF transmissions followed by no actions or non-active clinical actions (class 0 or 1); False -: Negative partners-HF transmissions followed by active clinical actions (class 2 or 3); B: True +: Positive care alert transmissions followed by active clinical actions (class 2 or 3); False +: Negative care alert transmissions followed by no actions or non-active clinical actions (class 0 or 1); True -: Positive care alert transmissions followed by no actions or non-active clinical actions (class 0 or 1); False -: Negative care alert transmissions followed by active clinical actions (class 2 or 3). All values are expressed in terms of percentage of total transmissions. HF: Heart failure.

> 60 plus one of the following parameters: reduced HRV (13.6%), low PA (12.3%), or reduced %CRT (11%); and (5) The most common active clinical action was HF-therapy titration, particularly of diuretics and beta-blockers, and the introduction of oral anticoagulation in patients with asymptomatic AF.

Despite advances in treatment of HF, it is still a major cause of cardiovascular mortality and hospitalization, especially in the early period after hospital discharge[1]. Prevention of HF relapses is important not only to reduce HF mortality and morbidity, but also health care costs[1]. Cardiac implantable electronic devices have nowadays remote monitoring capabilities that allow clinicians to have remote access to the complete device diagnostic information.

Previous studies
Earlier studies have shown that implantable device-measured variables, including intra-thoracic impedance, AF burden, mean heart rate, HRV, PA, frequency of PVCs, VA episodes, ICD shocks and %CRT, indivi-

duate subjects at risk of HF and facilitate early interventions[6-10]. Intrathoracic impedance[3], HRV and PA[2] reduction, occurs nearly two weeks before HF exacerbation. Low HRV indicate a sympathetic dominance in cardiac autonomic control and may be associated with exacerbation of atrial and VAs[13]. A prolonged AF duration, a rapid VR during AF and an increase in the burden of PVCs reduce %CRT[14] and are warning signs of HF, together with ICD shocks[15].

Although validated in various studies, the use of each device parameter in HF patients, is restricted by some limitations. In particular, variations of intrathoracic impedance may be related to lung inflammation; increased AF burden and prolonged AF duration are not useful in subjects with permanent AF; reduced mean heart rate, HRV or patient activity may reflect difficulty walking secondary to orthopedic diseases. Consequently, there is great interest in combining HF device diagnostic parameters for the management of CRT-D recipients.

The partners-HF[11] was a large cohort study explor-

ing the ability of the partners-HF criteria algorithm to dynamically stratify patients' risks of HF. A cohort of 694 CRT-D recipients with advanced HF (NYHA Ⅲ-Ⅳ) was prospectively evaluated in 100 centers. The retrospective evaluation of diagnostic CRT-D data demonstrated that subjects with a positive partners-HF algorithm had greater risk of hospitalization due to HF in the next month (adjusted HR = 5.5; $P < 0.001$). Moreover, the study demonstrated that increasing the frequency of reviewing the HF device diagnostics from quarterly (90 d) to monthly (30 d) but not to semimonthly (15 d), improved the ability to identify individuals at higher HF risk.

The prospective, multicenter observational Home Monitoring in CRT (Home-CARE) study[16] followed up for 1 year 377 CRT-D recipients who had been hospitalized for HF at least once within the 12 mo before enrollment. The following data were automatically retrieved every 24 h by the Home Monitoring (Biotronik, Berlin, Germany) algorithm: Mean heart rate, heart rate at rest, PA, frequency of PVCs, HRV, right ventricular pacing impedance, and painless shock impedance. The retrospective sensitivity values of individual parameters ranged from 23.6% to 50.0%, whereas their combination displayed 65.4% sensitivity and 99.5% specificity for cardiovascular hospitalizations and deaths.

Some studies have demonstrated favorable effects of RM in improving HF treatment, with potential benefits on clinical outcomes[6-10]. However, few and inconclusive data are available on the RM use in routine clinical practice and its impact on HF clinical outcomes. The Home Guide[17] registry proved RM highly effective in detecting clinical events, excluding deaths, with a sensitivity and a positive predictive values of 89% and 97%, respectively. RM sensitivity for atrial and VAs and device-related issues was > 90%, while it was < 35% for stroke, syncope and acute coronary syndromes and displayed an intermediate sensitivity (59%) for HF detection. Interestingly, 3 out of 4 events needing clinical intervention were asymptomatic and were effectively detected by RM, allowing a prompt reaction.

In our study the most common clinical reaction to partners-HF transmissions was drug therapy adjustment, while HF therapy titration and oral anticoagulation introduction in patients with asymptomatic AF were the most prevalent therapy interventions.

Clinical implications
This is the first multicenter observational registry prospectively assessing the clinical utility of partners-HF algorithm for risk stratification of HF patients in clinical practice. Remote monitoring of CRT-D recipients trough partners-HF algorithm, was not compared with usual care and this registry was not powered to explore the impact of the partners-HF algorithm on HF-hospitalizations and mortality. Our results prove that the partners-HF has significant diagnostic accuracy in determining active clinical actions oriented to treat pre-HF status and to prevent an acute decompensation.

Given the high positive and very high negative predictive values, clinicians could contact only patients with positive partners-HF transmissions, thus avoiding a significant number of unnecessary telephone contacts.

Care alert displays very low sensitivity and a poor ability to identify patients needing active clinical action oriented to treat pre-HF status. Moreover, given its low positive predictive value, clinicians should be aware that an active clinical action oriented to preventing acute HF may be not necessary in case of care alert triggered transmissions.

Another important aspect is that this prospective analysis was conducted in patients with advanced HF (82.7%: NYHA classes Ⅲ/Ⅳ; mean EF: 27.5% ± 6.5%). This may explain the high percentage of manual and care alert transmissions collected and the high prevalence of positive partners-HF transmissions (35%). Considering that no HF hospitalization occurred in a population of advanced HF during a 6 mo follow-up, the partners-HF algorithm appears to be a powerful tool to identify and consequently treat pre-HF status in order to prevent acute decompensation.

According to the partners-HF study[11], positive partners transmissions were mostly triggered by the optivol fluid index, alone or in combination with low HRV, low PA or a low %CRT. The weight of each partners-HF criterion in the risk stratification of HF patients was not considered in this registry. A combined algorithm of HF diagnostic parameters could be utilized to stratify patients into high, medium and low risk of HF by using a specific risk stratification score, calculated by attributing a specific weight to each partners-HF criterion on the basis of its ability to detect pre-HF status. Finally, whether therapeutic interventions based on the partners-HF algorithm are effective in improving outcomes in HF, was not investigated.

The partners-HF algorithm proved to be a powerful predictor of a pre-HF status and was able to guide clinical actions oriented to avoiding acute HF. Future larger randomized prospective trials should be performed to confirm our results, to develop and validate a dynamic HF risk score based on the partners-HF algorithm and to ascertain whether the use of this algorithm for RM can improve the main clinical outcomes of HF patients.

COMMENTS

Background
Heart failure (HF) is a principal cause of death hospitalization and health care costs. The partners-HF algorithm retrospectively identified cardiac resynchronization-defibrillator (CRT-D) recipients at risk of HF relapses in the subsequent 30 d. However no studies have validated this algorithm prospectively and have compared it with the care alert strategy, that is commonly adopted for CRT-remote monitoring.

Research frontiers
Remote monitoring has emerged as a useful tool to prevent HF relapses, and to reduce cardiac hospitalization and mortality.

Innovations and breakthroughs
This is the first multicenter observational registry prospectively assessing the

clinical utility of partners-HF algorithm for risk stratification of HF patients in clinical practice.

Applications
The authors' prospective study showed that the partners-HF algorithm has significant diagnostic accuracy in determining active clinical actions oriented to prevent HF relapses. Moreover, it has a high positive and a high negative predictive value, allowing clinicians to contact only patients with positive partners-HF transmissions, thus avoiding a significant number of unnecessary telephone contacts.

Terminology
Remote monitoring: Wireless remote monitoring of cardiac electronic devices, including cardiac defibrillators and CRT.

Peer-review
This is a valuable research, because status of clinical actions is very important for patient's therapy and outcomes. Herein the traits of the partners-HF algorithm *vs* care alert in determining active clinical actions were explored and observed the effect of different methods on treatment or prevent heart failure.

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