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SHORT COMMUNICATION

Serial heart rate measurement and mortality after acute heart failure

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Abstract

Aim Heart failure (HF) poses a unique medical burden of high morbidity and mortality. Elevated resting heart rate (HR) is associated with worse outcomes in chronic HF, but little is known about the prognostic impact of serial HR measurement during hospital stay after acute HF. We examined the association between HR obtained at admission at Day 4 and at discharge and long-term mortality in a cohort of 672 patients discharge from hospital after management of acute HF.

Methods and results All patients examined were in sinus rhythm. HR was derived from electrocardiogram and was defined as the first reported HR in the medical record. At 1 year follow up, 60 patients died. Median HR was 86 ± 17 b.p.m. (first tertile: 75 b.p.m., third tertile: 97 b.p.m.) at admission, 76 ± 14 b.p.m. (first tertile: 67 b.p.m., third tertile 85 b.p.m.) at Day 4, and 72 ± 11 b.p.m. (first tertile: 64 b.p.m., third tertile 80 b.p.m.) at discharge. Patients who died were significantly older (75 ± 11 vs. 71 ± 12 years; $P = 0.027$), had more frequently a history of ischemic cardiomyopathy ($n = 34/60$, $P = 0.012$) and of chronic obstructive pulmonary disease (n = 26/60, $P = 0.027$), had higher admission N terminal pro brain natriuretic peptide (14 572 ± 21 600 vs. 7647 ± 7964 pg/ml; $P = 0.027$), had lower systolic and diastolic blood pressures ($P < 0.05$), haemoglobin level (10.6 ± 2.2 vs. 12.2 ± 2.2 g/L; $P = 0.005$), albumin level (35.2 ± 4.3 vs 37.1 ± 4.1 g/dl; $P = 0.003$) and estimated glomerular filtration rate (47 ± 21 vs. 60 ± 28 ml/min/1.73 m^2; $P = 0.0017$). There were no significant differences between survivors and nonsurvivors in left ventricular ejection, the use of beta-blocker and angiotensin-converting enzyme-inhibitor, and the rate of comorbidities (hypertension, diabetes) (P=NS, for all). HR at admission was not significantly associated with 1 year mortality ($P = 0.20$), whereas there was a significant increase in 1 year mortality for HRs>85 b.p.m. at Day 4 ($P < 0.0001$) and > 80 b.p.m. at discharge ($P < 0.0001$). In the multivariable model that included the third tertile at Day 4 and discharge HR and adjusted for all other significant covariates, haemoglobin ($P = 0.019$), and HR at Day 4 ($P = 0.023$) were independently associated with 1 year mortality. When only discharge HR was included haemoglobin ($P = 0.0004$) and HR at discharge ($P = 0.00053$) remained independently associated with 1 year mortality.

Conclusions In patients surviving the acute HF phase, a high HR at Day 4, and at a lesser degree at discharge, but not at admission, is a strong predictor of 1 year mortality.

Keywords Heart failure; 1 Year mortality; Heart rate

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Introduction

Heart failure (HF) poses a unique medical burden of high morbidity and mortality. The continued high mortality rate for patients hospitalized with acute HF provides a compelling indication for accurate risk stratification to potentially improve individual management and hospital outcome. Elevated resting heart rate (HR) is associated with worse outcomes in chronic HF but little is known about the clinical value of serial HR measurement during hospital stay after acute HF.[1–4] The main aim of the present study was to examine the relationship between resting HR obtained at admission at Day 4 and at discharge and long-term mortality after surviving from acute HF.

Table 1 Comparison between baseline characteristics and 1 year mortality

Variable	Whole cohort (n = 672)	Survivors (n = 612, 91%)	Death (n = 60, 9%)	P
Age, years	72 ± 12	71 ± 12	75 ± 12	0.027
Heart rate at admission	86 ± 16	86 ± 17	88 ± 14	0.20
Systolic blood pressure at admission	122 ± 24	112 ± 19	123 ± 24	0.028
Diastolic blood pressure at admission	68 ± 13	63 ± 12	68 ± 13	0.036
Left ventricular ejection fraction, %	45 ± 16	42 ± 16	45 ± 16	0.09
Left ventricular ejection fraction < 40%, n (%)	283 (42)	251 (41)	31 (52)	0.30
Medical history				
Hypertension, n (%)	314 (47)	282 (46)	32 (53)	0.38
Diabetes, n (%)	118 (18)	107 (17)	11 (18)	0.96
COPD, n (%)	166 (25)	144 (24)	26 (43)	0.027
Ischaemic cardiomyopathy, n (%)	274 (41)	240 (39)	34 (57)	0.012
Medications				
ACE-inhibitor	245 (36)	221 (36)	24 (40)	0.55
Beta-blockers	269 (40)	243 (40)	26 (43)	0.58
Laboratory findings				
Haematocrite, %	37 ± 6	35 ± 6.6	38 ± 6	0.015
Haemoglobin, g/dl	12.1 ± 2.2	12.3 ± 2.2	11.3 ± 2.2	0.005
Albumin, g/L	36.9 ± 4.1	37.1 ± 4.1	35.3 ± 4.3	0.003
Total protein, g/L	64.8 ± 6.3	65 ± 5.8	65 ± 6.4	0.67
NT-proBNP, pg/ml	8488 ± 10660	7647 ± 7964	14572 ± 21600	0.027
Sodium, mmol/L	141 ± 4.2	141 ± 3.4	140.7 ± 4.3	0.65
Creatinine, mg/dl	14.0 ± 10.3	13.8 ± 10.3	16.4 ± 9.6	0.08
Estimated GFR, ml/min/mm^3	59.1 ± 28.0	60 ± 28	47 ± 21	0.0017
C-reactive protein, mg/L	**7.4 ± 2.8**	**7.5 ± 2.8**	**6.5 ± 1.2**	0.14

Abbreviations: ACE, angiotensin-converting enzyme; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate.

Methods

The present study collected detailed hospitalization data from computerized medical records of patients presenting with acute HF at CHU of Liège, Belgium, between January 2010 and December 2012. Patients (n = 1611) were eligible for the first round of selection if they were > 18 years of age, had a suspected diagnosis of HF, and were alive 24–36 h after admission. After a second round of selection, 899 patients with ≥1 following criteria were further disqualified respiratory support, cardiogenic shock, acute coronary syndrome, resting HR < 40 b.p.m., inotropic support, primary valvular heart disease, permanent pacemaker pacing, arrhythmias, infectious/inflammatory disease (C-reactive protein >10 mg/L), end-stage renal failure requiring dialysis, and cancer. At the end of the selection process, we kept 672 patients discharged from hospital after management of acute HF in whom serial HR measurement was reported in the medical file (no data on electrocardiogram morphology and adaptation of medication during the hospital stay were obtained). The association between HR obtained at admission at Day 4 and at discharge, and long-term mortality was then examined retrospectively. The diagnosis of HF was based upon the following conditions to be satisfied symptoms typical of HF, signs of HF, either reduced left ventricular ejection fraction or diastolic dysfunction with structural heart disease and increased N terminal pro brain natriuretic peptide (>125 pg/ml, median: 4954 pg/ml, 25-75th percentile 2362–12194 pg/ml). HR was derived from electrocardiogram and was defined as the first reported HR in the medical record. Hospital HR was categorized into tertiles. A logistic model was applied to identify significant predictors of 1 year mortality. All statistical analyses were performed with STATISTICA Version 10 (StatSoft Inc, Tulsa, Okla). In order to avoid overfitting the multivariable model, we have only included significant univariable parameters. Values of $P < 0.05$ were considered significant. All authors have read and agree to the manuscript as written. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Figure 1 Association of heart rate tertiles with 1 year mortality after acute heart failure. Adjusted odds ratio for significant covariates (see text). First tertile taken as referent in each group.

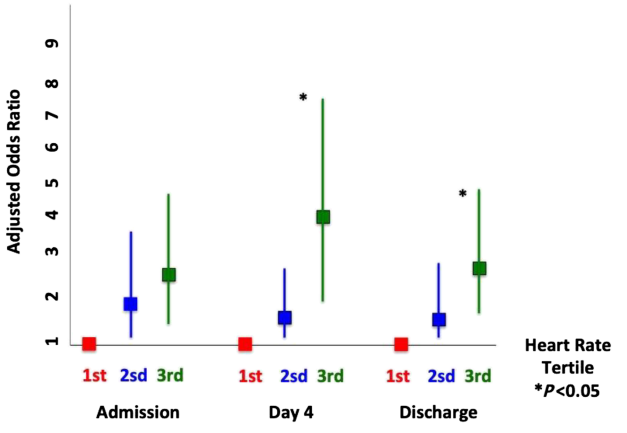

Table 2 Multivariable predictors of 1 year mortality (heart rate as continuous variables)

Heart rate at Day 4				Heart rate at discharge			
Variable	OR	95% CI	p	Variable	OR	95% CI	p
Age, per 1 year	0.97	0.94–1.01	0.26	Age, per 1 year	1.03	0.98–1.08	0.31
Heart rate at Day 4, per 1 b.p.m.	1.11	1.06–1.16	0.000007	Heart rate at discharge, per 1 b.p.m.	1.16	1.08–1.24	0.00004
Systolic blood pressure, per 1 mmHg	0.98	0.96–1.00	0.21	Systolic blood pressure, per 1 mmHg	1.00	0.98–1.02	0.91
COPD, yes versus no	1.52	0.47–4.91	0.48	COPD, yes versus no	0.93	0.24–3.6	0.92
Ischaemic cardiomyopath, yes versus no	1.49	0.48–4.62	0.41	Ischaemic cardiomyopath, yes versus no	0.33	0.33–1.22	0.10
Haemoglobin, per 1 g/dl	0.45	0.31–0.65	0.00002	Haemoglobin, per 1 g/dl	0.56	0.40–0.78	0.0006
Albumin, per 1 g/L	0.86	0.76–0.97	0.015	Albumin, per 1 g/L	0.82	0.75–0.89	0.02
NT-proBNP, per 1 pg/ml	1.026	0.97–1.08	0.31	NT-proBNP, per 1 pg/ml	1.09	0.91–1.29	0.35
Estimated GFR, per 1 ml/min/mm^3	0.96	0.94–0.98	0.0045	Estimated GFR, per 1 ml/min/mm^3	0.89	0.85–0.93	0.044

Abbreviations: CI, confidence interval; COPD, chronic obstructive pulmonary disease; GFR, glomerular filtration rate; NT-proBNP, N terminal pro brain natriuretic peptide; OR, odds ratio.

Results

All patients examined were in sinus rhythm. HR was 86 ± 17 b.p.m. (first tertile: 75 b.p.m., third tertile 97 b.p.m.) at admission, 76 ± 14 b.p.m. (first tertile: 67 b.p.m., third tertile 85 b.p.m.) at Day 4, and 72 ± 11 b.p.m. (first tertile: 64 b.p.m., third tertile 80 b.p.m.) at discharge (13 ± 6 days). At 1 year follow up, 60 patients died. Those patients were significantly older (75 ± 11 vs. 71 ± 12 years; $P = 0.027$), had more frequently a history of ischemic cardiomyopathy ($n = 34/60$, $P = 0.012$) and of chronic obstructive pulmonary disease ($n = 26/60$, $P = 0.027$), had higher admission N terminal pro brain natriuretic peptide (7647 ± 7964 vs. 14572 ± 21600; $P = 0.027$), had lower systolic and diastolic blood pressures ($P < 0.05$), haemoglobin level (12.2 ± 2.2 vs. 10.6 ± 2.2 g/dl; $P = 0.005$), albumin level (37.1 ± 4.1 vs. 35.2 ± 4.3 g/dl; $P = 0.003$) and estimated glomerular filtration rate (60 ± 28 vs. 47 ± 21 ml/min/1.73 m^2; $P = 0.0017$) (*Table 1*). There were no significant differences between survivors and nonsurvivors in left ventricular ejection, the use of beta-blocker and angiotensin-converting enzyme-inhibitor, and the rate of comorbidities (hypertension, diabetes) (P=NS, for all). HR at admission was not significantly associated with 1 year mortality [odds ratio (OR), 1.01; 95% confidence interval (CI), 0.90–1.03; $P = 0.20$], whereas HR at Day 4 (OR 1.05; 95%CI, 1.03–1.08; $P < 0.0001$) and at discharge (OR 1.09; 95%CI, 1.06–1.11; $P < 0.0001$) were predictive of the outcome. There was also a significant increase in 1 year mortality for HRs>85 b.p.m. at Day 4 (OR 3.2; 95% CI, 1.88–5.48; $P < 0.0001$) and > 80 b.p.m. at discharge (OR 3.1; 95% CI, 1.98–4.89; $P < 0.0001$) (*Figure 1*). Of note, when receiver operating characteristic curve analysis was used for predicting 1 year mortality, the best cut-off value for HR at Day 4 was 82 b.p.m. (AUC 0.77, 95%CI 0.74–0.80, sensitivity 64%, specificity 82%), and for HR at discharge was 78 b.p.m. (AUC 0.73, 95% CI 0.69–0.76, sensitivity 68%, specificity 68%). *Table 2* summarized the multivariable models when HR was included as a continuous variable at Day 4 and at discharge. In the multivariable model that included HR at Day 4 and at discharge, HR at discharge was no longer significant. In the multivariable model that included the third tertile at Day 4 and discharge HR and adjusted for all other significant covariates, haemoglobin (OR 0.74; 95% CI, 0.57–0.95; $P = 0.019$), and HR at Day 4 (OR 2.4; 95% CI, 1.1–5.1; $P = 0.023$) were independently associated with 1 year mortality. When only discharge HR was included, haemoglobin (OR 0.67; 95% CI, 0.53–0.84; $P = 0.0004$) and HR at discharge (OR 2.4; 95% CI, 1.5–3.8; $P = 0.00053$) remained independently associated with 1 year mortality.

Conclusions

For the first time, we showed that in patients surviving the acute HF phase, a high HR at Day 4, and at a lesser degree at discharge, but not at admission, was a strong predictor of 1 year mortality. Specifically, HRs exceeding 85 b.p.m. were associated with higher mortality while lower thresholds portended better prognosis. Elevated HR results from sympathetic overactivity and is associated with plaque vulnerability and increased oxygen consumption and reduced diastolic filling times, thus compromising coronary perfusion with induction of myocardial ischemia, and precipitation of rhythm disturbances. Early targeting of elevated HR may therefore represent a complementary therapeutic challenge in these patients.[5] However, in practice, the main therapeutic goal is not so much to directly modulate the HR but to swiftly manage HF symptoms and the increased sympathetic activity by the rapid initiation of effective HF medical treatment (vasodilator, diuretics, and oxygen). In some cases, continuing a tailored dose of beta-blocker with a rapid uptitration during the acute HF phase may also be effective.[4] Noteworthy, the most appropriate HR to target is likely that around Day 4 rather than discharge HR because this latter is probably not associated with clinical benefits.[5] Our findings highlight opportunities for risk stratification and intervention that will require further investigation.

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Conflict of interest

All the authors have no disclosure related to this study.

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