Original Scientific Paper

Relation of heart rate recovery to psychological distress and quality of life in patients with chronic heart failure
Roland von Känela,b, Hugo Sanera, Sonja Kohlsa, Jürgen Barthc, Hansjörg Znojd, Gaby Sanera and Jean-Paul Schmida

aCardiovascular Prevention and Rehabilitation, bDivision of Psychosomatic Medicine, Bern University Hospital, Inselspital, cInstitute of Social and Preventive Medicine and dClinical Psychology and Psychotherapy, University of Bern, Switzerland

Received 23 October 2008 Accepted 21 January 2009

Background Psychological distress, poor disease-specific quality of life (QoL), and reduction in vagally mediated early heart rate recovery (HRR) after exercise, all previously predicted morbidity and mortality in patients with chronic heart failure (CHF). We hypothesized lower HRR with greater psychological distress and poorer QoL in CHF.

Design All assessments were made at the beginning of a comprehensive cardiac outpatient rehabilitation intervention program.

Methods Fifty-six CHF patients (mean 58 ± 12 years, 84% men) completed the Hospital Anxiety and Depression Scale and the Minnesota Living With Heart Failure Questionnaire. HRR was determined as the difference between HR at the end of exercise and 1 min after exercise termination (HRR-1).

Results Elevated levels of anxiety symptoms (P=0.005) as well as decreased levels of the Minnesota Living With Heart Failure Questionnaire total (P=0.025), physical (P=0.026), and emotional (P=0.017) QoL were independently associated with blunted HRR-1. Anxiety, total, physical, and emotional QoL explained 11.4, 8.0, 7.8, and 9.0%, respectively, of the variance after controlling for covariates. Depressed mood was not associated with HRR-1 (P=0.20).

Conclusion Increased psychological distress with regard to elevated anxiety symptoms and impaired QoL were independent correlates of reduced HRR-1 in patients with CHF. Reduced vagal tone might explain part of the adverse clinical outcome previously observed in CHF patients in relation to psychological distress and poor disease-specific QoL. Eur J Cardiovasc Prev Rehabil 16:645–650 © 2009 The European Society of Cardiology

Keywords: autonomic function, cardiovascular disease, exercise, psychological stress

Introduction
Patients with chronic heart failure (CHF) showed blunted post-exercise heart rate recovery (HRR) [1], which, in turn, predicted hospitalizations because of heart failure [2], composite death/hospitalization end-point [3], and all-cause mortality [4,5]. Heart rate decline during the first minute of recovery from exercise (HRR-1) predominantly reflects parasympathetic activation, whereas HRR measured after this period is additionally affected by gradual sympathetic withdrawal after termination of exercise [6]. Moreover, HRR-1 can preferentially be used to approximate overall vagal tone of the human organism [6,7].

Psychological distress is high and quality of life (QoL) is low in patients with CHF [8,9]. Particularly increased levels of anxiety and depressive symptoms predicted mortality in CHF patients [10–12]. In addition, poor disease-specific total, physical, and emotional QoL, as assessed by the Minnesota Living With Heart Failure Questionnaire (MLWHQ), was an independent predictor of heart failure hospitalization and all-cause mortality [13,14]. Impaired autonomic function may link
psychological distress, including anxiety and depression, with cardiac morbidity and mortality [15]. In agreement with this literature, earlier studies found an inverse association between levels of depressed mood and HRR in patients with coronary artery disease [16]. To our knowledge, it has not been explored whether psychological distress and QoL are related to HRR in patients with CHF.

We hypothesized that elevated levels of anxiety and depression on one hand and decreased levels of QoL on the other would be associated with reduced HRR-1 in patients with CHF. We further hypothesized that these relationships would be independent of other correlates of reduced HRR such as female sex [17], older age [17,18], elevated body mass index (BMI) [19], decreased left ventricular ejection fraction (LVEF) [5], lowered exercise capacity [18], and peak heart rate (HR) during exercise [18].

Methods

Patients and recruitment
The study protocol was approved by the ethical committee of the State of Bern, Switzerland. All patients provided written informed consent. The study sample comprised 56 consecutively enrolled patients with ischemic and nonischemic CHF, who received first-time outpatient cardiac rehabilitation at the Cardiac Prevention and Rehabilitation Clinic of the University Hospital of Bern, Switzerland. Inclusion criteria were primary diagnosis of clinically stable heart failure, LVEF ≤ 40% during echocardiography, no electrocardiographic signs of atrial fibrillation or atrial flutter, and HRR-1 ≥ 1 beats/min (bpm). All demographic, medical, and questionnaire data were obtained through a history and standardized assessments at entry of a 12-week comprehensive rehabilitation program tailored to the needs of patients with CHF.

Psychological distress and quality of life

Anxiety and depression
Patients completed the 14-item German version of the Hospital Anxiety and Depression Scale (HADS) [20]. Each item is rated on a four-point Likert scale (range from 0 = 'mostly' to 3 = 'not at all'). The seven-item subscales for anxiety (HADS-A) and depression (HADS-D) yield a score of 0–21 points. The HADS is a valid screening tool to detect anxiety and depression in CHF outpatients [21]. Two patients did not complete one item of the HADS-D. These missing values were replaced by the mean of an individual's completed items.

Quality of life
Patients completed the German version of the 21-item MLWHQ to assess disease-specific QoL [22]. The questionnaire asks about how much the heart condition affected the patient’s life during the past month. Each item is rated on a Likert scale between 0 (no impairment) and 5 (very much impaired) resulting in a total score between 0 and 105 for total QoL. The MLWHQ also allows one to compute subscores for the physical (eight items, range 0–40) and emotional (five items, range 0–25) dimensions of QoL. Two patients did not complete the MLWHQ leaving 54 patients for the QoL analysis. Five, three, one, and two patients, respectively, lacked one, two, three, and four items. Missing values were replaced by the mean of an individual’s completed items.

Exercise testing and heart rate recovery
Patients underwent symptom-limited incremental exercise testing on a computer-controlled, rotational, speed independent bicycle ergometer (Ergo-metrics 800S; Ergoline GmbH, Bitz, Germany) following a standard protocol while kept on their medication. After a 3-min reference phase, during which patients cycled without a workload, the test phase began with a 10 W/min ramp protocol until volitional dyspnoe or muscle fatigue forced cessation of the exercise. A 12-lead electrocardiogram was continuously recorded. To obtain a measure of HRR-1, HR at 1 min of passive recovery was subtracted from the HR at the end of exercise [6]. We also recorded peak HR during exercise and maximal exercise capacity.

Data analyses
Data were analyzed using SPSS (version 15.0, SPSS Inc., Chicago, Illinois, USA) with level of significance set at \( P \leq 0.05 \) (two-tailed). The scores for depressed mood and emotional QoL were logarithmically transformed to achieve a normal distribution before performing analyses. All data are presented in original units for clarity. Pearson correlation analysis was used to estimate the univariate relationship between two variables. Linear regression analysis was used to test whether psychological factors were significantly linked with HRR-1, independent of covariates. All covariates, including psychological factors were forced entry in one block into the regression equation.

### Table 1: Characteristics of the 56 chronic heart failure patients studied

<table>
<thead>
<tr>
<th>Men (%)</th>
<th>Age (years)</th>
<th>Body mass index (kg/m²)</th>
<th>Left ventricular ejection fraction (%)</th>
<th>Beta-blocker use (%)</th>
<th>Systolic blood pressure (mmHg)</th>
<th>Diastolic blood pressure (mmHg)</th>
<th>HADS anxiety score</th>
<th>HADS depression score</th>
<th>MLWHQ total quality of life score</th>
<th>MLWHQ physical quality of life score</th>
<th>MLWHQ emotional quality of life score</th>
<th>Maximum exercise capacity (W)</th>
<th>Peak heart rate during exercise (beats/min)</th>
<th>Heart rate recovery-1 (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>84</td>
<td>58.0 ± 12.0</td>
<td>26.6 ± 4.9</td>
<td>36.5 ± 7.2</td>
<td>95</td>
<td>111.8 ± 18.3</td>
<td>71.4 ± 9.8</td>
<td>4.5 ± 3.4</td>
<td>4.0 ± 3.8</td>
<td>31.9 ± 19.3</td>
<td>14.6 ± 9.9</td>
<td>63.5 ± 5.8</td>
<td>105.0 ± 36.2</td>
<td>128.8 ± 22.1</td>
<td>189.9 ± 8.7</td>
</tr>
</tbody>
</table>

Values are given as means ± SD or in percentages. HADS, Hospital anxiety and depression scale; Heart rate recovery-1, decline in heart rate from end of exercise to 1 min recovery; MLWHQ, Minnesota Living With Heart Failure Questionnaire.
Results

Patient characteristics

Table 1 shows the characteristics of the patients. Clinically elevated anxiety and depression levels (≥ 8 points) each were found in 12 patients (21%), whereas no patient showed severely elevated scores of anxiety or depression (all scores ≤ 13). Virtually all patients were under treatment with β-blockers. Total QoL correlated with anxiety (r = 0.56) and depression (r = 0.56) and anxiety and depression were also correlated (r = 0.70) (all P values < 0.001).

Prediction of heart rate recovery

Bivariate analysis

There were significant relationships between HRR-1 and anxiety (r = -0.37, P = 0.005; Fig. 1a), total QoL (r = -0.37, P = 0.006; Fig. 1b), physical QoL (r = -0.38, P = 0.005; Fig. 1c), and emotional QoL (r = -0.38, P = 0.004; Fig. 1d) indicating that elevated anxiety and poorer QoL were associated with a smaller decline of HR in the first minute after exercise. HRR-1 and symptoms of depression were not associated with each other (P = 0.18). In addition, there were no relationships

Fig. 1

Psychological factors and heart rate recovery after exercise. The regression plots with fit line show the significant bivariate associations between reduced heart rate recovery in the first minute after exercise and higher levels of anxiety (a), poorer total quality of life (b), poorer physical quality of life (c), and poorer emotional quality of life (d). HADS, Hospital Anxiety and Depression Scale; MLWHQ, Minnesota Living With Heart Failure Questionnaire. Note that higher scores on the MLWHQ mean poorer disease-specific quality of life. R^2 linear, R square (explained variance).
between HRR-1 and sex ($P = 0.62$), age ($P = 0.34$), BMI ($P = 0.38$), LVEF ($P = 0.98$), β-blocker use ($P = 0.60$), systolic blood pressure ($P = 0.44$), and diastolic blood pressure ($P = 0.16$). HRR-1 correlated with peak HR during exercise ($r = 0.42$, $P = 0.001$) and, with a trend towards statistical significance, also with maximum exercise capacity ($r = 0.22$, $P = 0.10$).

**Controlled multivariate analysis**

**Anxiety** Anxiety scores were independently associated with lower HRR-1 ($\beta = -0.36$, $P = 0.005$) after controlling for sex ($P = 0.27$), age ($P = 0.66$), BMI ($\beta = 0.22$, $P < 0.09$), LVEF ($P = 0.16$), maximum exercise capacity ($P = 0.94$), and peak HR ($\beta = 0.43$, $P = 0.002$). The unstandardized coefficient B revealed a reduction in HRR-1 of $-0.92 \pm 0.32$ bpm with each point increase on the HADS-A scale. The entire model explained 35.9% ($P = 0.002$) of the variance ($R^2$) in HRR-1. Anxiety symptoms individually explained a significant 11.4% ($AR^2$) of the variance in HRR-1 after controlling for all covariates.

**Depression** Levels of depressed mood showed no independent association with HRR-1 when all covariates were taken into account ($\beta = -0.17$, $P = 0.20$). The entire model explained 27.1% of the variance in HRR-1 ($P = 0.026$).

**Quality of life** After controlling for sex ($P = 0.71$), age ($P = 0.74$), BMI ($\beta = 0.23$, $P < 0.08$), LVEF ($P = 0.25$), maximum exercise capacity ($P = 0.93$), and peak HR during exercise ($\beta = 0.40$, $P = 0.008$), poorer total QoL was independently associated with lower HRR-1 ($\beta = -0.30$, $P = 0.025$). There was a reduction in HRR-1 of $-0.14 \pm 0.06$ bpm with each point increase (i.e. reflecting decrease in QoL) on the MLWHQ total score. The entire model explained 32% of the variance in HRR-1 ($P = 0.009$). The total QoL scores explained a significant 8.0% of the variance in HRR-1 after controlling for all covariates.

A significant independent relationship also emerged between HRR-1 and physical QoL ($\beta = -0.31$, $P = 0.026$) and emotional QoL ($\beta = -0.32$, $P = 0.017$) explaining a significant 7.8 and 9.0%, respectively, of variance after taking into account all covariates. For each point increase in the physical and emotional score of the MLWHQ (i.e. reflecting a decrease in QoL in these dimensions), there was a reduction in HRR-1 of $-0.28 \pm 0.12$ and $-0.45 \pm 0.20$ bpm, respectively.

**Discussion**

We found that elevated levels of anxiety and impaired disease-specific QoL both related to blunted HRR during the first minute after exercise termination in patients with CHF. These effects were observed in bivariate analyses and remained statistically significant after controlling for previously observed correlates of HRR. Anxiety explained more than 11% of the individual variance in HRR-1. This seems a clinically meaningful effect to be illustrated as follows. For three point increase on the anxiety scale, our patients experienced a 3-bpm decrease in their HRR-1. The average HRR-1 was 19 bpm in our patients. In patients referred for exercise echocardiography, a decline in HRR-1 of 3 bpm, which is from 25 to 22 to 19 bpm, and to $\leq 16$ bpm predicted an average increase in 3-year mortality rate of 2, 4, 6, and 9% respectively [23].

Depression was not significantly associated with HRR-1. This finding contrasts the widely accepted notion that depression is characterized by altered autonomic function [15]. However, much of this literature investigated heart rate variability measures of vagal cardiac control [15], whereas early HRR after exercise may be a more suitable index of overall vagal tone [9]. A relatively low level of depressed mood in our patients could also explain why depression showed no association with HRR-1. The mean HADS-D score of our patients was 4.0, which is particularly lower than the average HADS-D score of 6.4 previously shown to predict mortality in CHF patients at 2-year follow-up [24].

Impairment in the total disease-specific QoL was associated with lower HRR-1. Given that low perceived QoL (assessed by the MLWHQ) previously limited physical effort during exercise partially independent of physiologic function [25], it seemed particularly important to control for maximum exercise capacity in our study. In addition, we found that physical and emotional QoL were significantly associated with reduced HRR-1. These two domains of disease-specific QoL explained a similar amount of variance in HRR-1 although somewhat less than was explained by anxiety.

This study is, to our knowledge, the first to investigate the relation of HRR to psychological factors in CHF. Despite its intriguing findings, we acknowledge several limitations of our study. We controlled several potentially important correlates of HRR, but our sample size did not allow us in making adjustments for additional variables potentially affecting autonomic function pertinent to cardiovascular disease risk [26]. Therefore, the possibility remains that some of the variance in HRR-1 explained by anxiety and QoL are because of underlying third factors (e.g. somatic comorbidity and life style). Our sample included predominantly men and virtually all patients were treated with β-blocking drugs. Although we controlled for sex and there is some controversy as to whether β-blockers affect HRR [5,27,28], our findings might not be transferable to samples including a higher proportion of women patients and patients without β-blocker therapy. Nonetheless, HRR-1 maintained...
prognostic value for cardiac-related deaths in patients with CHF irrespective of β-blocker use [29]. Beta blockade had also minimal impact on the prognostic power of HRR for future cardiovascular mortality in male veterans [30]. As our study was cross-sectional, prospective design is needed to disentangle add-on, interactive, and unidirectional effects between psychological factors, QoL, and HRR in CHF in terms of their predictive value for clinical outcome [9]. Sophisticated statistical modeling in larger samples might also help us to better understand the pathways leading from psychological distress to QoL and vagal function or vice versa. For instance, in patients with CHF and coronary artery disease, respectively, exercise rehabilitation led to an increase in HRR with long-term effects [31,32] and improvement in QoL [33]. As exercise regimens are a standard element of cardiac rehabilitation programs tailored to CHF patients, a study on whether reduction in psychological distress and improvement in QoL resulting from rehabilitation act as a mediator or moderator of an increase in HRR seems warranted. Eventually, QoL is a complex concept shaped by situative factors and an individual’s perception and interpretations about the meaning of QoL; these issues might only sufficiently be tracked by a questionnaire. Moreover, future studies may want to investigate whether other biological measures, such as inflammation and sympathetic nervous system function, are related to QoL.

To sum up, given the significant and also clinically meaningful relationship between the psychological variables studied here and HRR-1, decreased vagal tone might help to explain some of the mortality risk in CHF patients previously predicted by anxiety and poor QoL. Whether our findings obtained in a sample of CHF patients scheduled to receive outpatient cardiac rehabilitation also transfer to a more diverse population of patients with CHF and even to patients with other cardiac diseases remains to be explored.

Acknowledgement
Conflict of interest: none declared.

References
18 Brinkworth GD, Noakes M, Buckley JD, Clifton PM. Weight loss improves heart rate recovery in overweight and obese men with features of the metabolic syndrome. Am Heart J 2006; 152:693.e1–693.e6.


