

# Effect of psychosocial factors on autonomic nervous system activity in patients with heart failure

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## Abstract

Autonomic imbalance predicts worse clinical outcomes in patients with heart failure (HF). Managing the variables affecting heart rate variability (HRV) might improve the clinical outcomes of patients with HF. This study aimed to investigate variables affecting HRV. We assessed autonomic nervous system activity (low-frequency [Lf], high-frequency [Hf], and Lf/Hf ratio) in 60 patients with HF, employing standard measures to capture short-term HRV. To estimate the independent effects of variables such as well-known cardiac risk factors and psychosocial conditions on HRV, multivariate analyses were conducted. For psychosocial variables, we assessed depression and quality of life in patients and their family caregivers. We also assessed the self-care behavior of patients and their caregivers' burden. Depression in family caregivers and self-care behavior of patients were independently associated with a decreased Hf ( $\beta$ -coefficient = 0.309,  $P = .039$  and  $\beta$ -coefficient =  $-0.029$ ,  $P = .047$ , respectively). Depression of family caregivers and self-care behavior of patients may affect HRV in patients with HF.

**Abbreviations:** HF = heart failure, Hf = high-frequency, HRV = heart rate variability, Lf = low-frequency, QoL = quality of life.

**Keywords:** autonomic nervous system activity, depression, heart failure, heart rate variability

## 1. Introduction

Despite advances in heart failure (HF) management, morbidity and mortality rates remain high.<sup>[1]</sup> Many studies have investigated prognostic factors for risk stratification in patients with HF.

Autonomic imbalance, characterized by generalized sympathetic overactivity and parasympathetic withdrawal, plays a significant role in the aggravation of symptoms and disease progression in patients with HF.<sup>[1,2]</sup> The analysis of heart rate variability (HRV) is a well-established prognostic factor in patients with HF.<sup>[3,4]</sup>

Psychosocial factors, such as depression and anxiety, can also influence HRV,<sup>[5,6]</sup> which is more prevalent in patients with HF than in general population.<sup>[7]</sup> Managing these psychosocial factors may improve clinical outcomes of patients with HF.

This study aimed to investigate the variables, including psychosocial factors, affecting HRV in patients with HF.

## 2. Materials and methods

This study employed a cross-sectional correlational design. We included adult patients (aged > 18 years of age) diagnosed with HF by a cardiologist and receiving regular medical follow-up. We enrolled patients who were considered clinically stable, without physical signs or symptoms suggestive of worsening cardiac function. Family caregivers were eligible to participate if they were adults over 18 years of age and accompanied a patient to the outpatient clinic as their primary family caregiver. Patients with HF and their respective family caregivers who assisted with daily activities were consecutively recruited from 2 university hospitals in Korea. As no previous study exists, we tried to enroll as many cases as possible within a certain period to enhance the statistical power and minimize both type I and type II errors. The study protocol and informed consent forms were reviewed and approved by the Institutional Review Board of each participating hospital (approval numbers: AJIRB-MED-SUR-18-214 and 3-2019-0121, respectively).

K-WS and J-Ah contributed equally to this work.

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To assess the short-term HRV of 60 patients with HF, we conducted a 5-minute test using a pulse wave analyzer (UBioClip v70; Biosense Creative Co., Ltd., Seoul, Korea). We measured autonomic nervous system activity, including sympathetic nerve activity (low-frequency [Lf]), parasympathetic nerve activity (high-frequency [Hf]), and autonomic nerve balance (ratio of Lf/Hf).

We assessed depression and quality of life (QoL) as psychosocial variables in both patients and their family caregivers. We also evaluated the self-care behavior of patients and caregivers' burden. Depression was assessed by using the geriatric depression scale, a 15-item questionnaire that identifies depressive symptoms.<sup>[8]</sup> A score exceeding 5 points indicated depression, with higher scores suggesting greater symptom severity. To assess QoL, a brief version of the World Health Organization Quality of Life Assessment Instrument, a 26-item questionnaire assessing individuals' perceptions of their health and well-being, was used.<sup>[9]</sup> Higher scores indicate better QoL. A critical value of 60 was identified as the optimal cut off point for assessing perceived QoL and satisfaction with health. Additionally, we used the European Heart Failure Self-care Behaviour Scale, a 12-item questionnaire, to evaluate patients' self-care behavior in managing their HF.<sup>[10]</sup> Higher scores indicated better self-care, with a score of >70 considered adequate. The objective burden on family caregivers was assessed using the Montgomery-Borgatta Caregiver Burden Assessment Scale, a 22-item questionnaire that use a 5-point Likert scale.<sup>[11]</sup> The questions included inquiries about objective burden, which pertains to the perceived disruption of tangible aspects of a caregiver's life, and subjective burden, which focuses on the emotional impact of caregiving responsibilities on caregivers. The higher the score, the greater the caregiver's burden. A value of less than 20 indicated little or no burden.

SPSS version 18.0 (SPSS, Chicago, IL) was used for all calculations. Continuous variables are presented as mean  $\pm$  standard deviation, categorical variables are shown as numbers and percentages. We conducted comparisons using the unpaired Student *t* test and ANOVA for continuous variables and Pearson's chi-square test for categorical variables. To estimate and test the independent effects of variables, like well-known cardiac risk factors and psychological conditions on autonomic nervous system activity, we employed multivariate analyses using linear regression. The normality assumption was assessed using Shapiro–Wilk test. Autonomic nervous system activity, including sympathetic nerve activity (Lf), parasympathetic nerve activity (Hf) and autonomic nerve balance (Lf/Hf ratio), was normally distributed ( $P = .07, .747, \text{ and } .096$ , respectively). We rigorously adhered to the following basic assumptions of the linear regression equation: linearity, independence, continuity, normality, homoscedasticity, absence of autocorrelation, and identification of outliers. We rejected null hypotheses of no difference when  $P$  values were  $< .05$ .

### 3. Results

The study included 60 patients (32 males,  $72 \pm 13$  year-old) with HF and their family caregivers (19 males,  $57 \pm 13$  year-old). The baseline clinical characteristics are summarized in Table 1. The mean duration from the primary diagnosis of HF to enrollment was  $5.7 \pm 5.9$  years. The number of hospitalizations for HF was  $1.5 \pm 1.9$ . Cardiac readmission was defined as any subsequent admission due to various causes related to the heart. The enrolled patients were considered clinically stable (New York Heart Associations classification,  $2.2 \pm 0.9$ ). Patients' and family caregivers' average depression scores were  $5.6 \pm 4.3$  and  $4.8 \pm 4.1$  (out of 15), respectively, indicating mild depressive symptoms in all participants. The total mean scores of QoL of patients and family caregivers were  $64.8 \pm 12.7$  and  $66.1 \pm 8.6$  (out of 156), respectively. All participants were

relatively satisfied with their QoL. The total mean score of self-care behavior of patients was  $39.1 \pm 6.1$  (out of 100), indicating inadequate self-care. The total mean score of caregivers' burden was  $57.9 \pm 9.1$  (out of 88), indicating a moderate to severe level of burden.

Multivariate logistic regression analyses of the clinical and psychosocial variables for autonomic nervous system activity are presented in Tables 2 to 4. There were no statistically significant differences between clinical and psychosocial variables and the parameters of increased sympathetic nerve activity and autonomic nerve balance (Tables 2 and 4). Depression of family caregivers and self-care behavior of patients were independently associated with decreased parasympathetic nerve activity ( $\beta$ -coefficient = 0.309,  $P = .039$  and  $\beta$ -coefficient =  $-0.029$ ,  $P = .047$ , respectively, Table 3).

### 4. Discussion

The present study demonstrated that depression in family caregivers and self-care behavior of patients were independently associated with autonomic imbalance, especially parasympathetic withdrawal.

In patients with HF, reduced parasympathetic sensitivity and inhibition of the parasympathetic nervous system are associated with poor prognosis.<sup>[12,13]</sup> Treatments targeting adrenergic receptor blockade, which inhibits adrenergic activity, enhances parasympathetic activity, or preferably, accomplishes both, play a pivotal role in improving clinical outcomes for patients with HF.<sup>[14–16]</sup> Stimulation of the carotid baroreceptor with baroreflex activation therapy results in a centrally mediated reduction in sympathetic outflow and increased parasympathetic activity, resulting in increased arterial and venous compliance and reduced peripheral resistance.<sup>[17]</sup> The present study demonstrated that depression in family caregivers and the self-care behavior of patients were closely related to parasympathetic withdrawal. Managing these psychosocial factors could be another therapeutic strategy for improving the prognosis of patients with HF.

While pharmacological and device-based interventions have yielded significant progress, morbidity and mortality associated with HF remain high.<sup>[1]</sup> This study focused on chronically stable patients receiving optimal medical treatment, and no clinical variables, except for psychosocial factors, were associated with HRV. Consistent with our findings, other studies have shown the influence of psychosocial factors on HRV.<sup>[15,6]</sup> Self-care behavior

**Table 1**  
Baseline characteristics.

Variables	Mean $\pm$ standard deviation (n = 60)
Clinical variables	
Age (year-old)	72 $\pm$ 13
Men, n (%)	32 (53%)
Duration of heart failure (yr)	5.7 $\pm$ 5.9
Hospitalization due to heart failure (n)	1.5 $\pm$ 1.9
NYHA classification	2.2 $\pm$ 0.9
Autonomic nervous system activity	
sympathetic nerve activity (Lf)	6.5 $\pm$ 2.1
parasympathetic nerve activity (Hf)	5.9 $\pm$ 1.5
autonomic nerve balance (Lf/Hf)	1.1 $\pm$ 0.2
Psychosocial variables	
Depression of patients (score)	5.6 $\pm$ 4.3
QoL of patients (score)	64.8 $\pm$ 12.7
Self-care behavior of patients (score)	39.1 $\pm$ 6.1
Depression of family caregivers (score)	4.8 $\pm$ 4.1
QoL of family caregivers (score)	66.1 $\pm$ 8.6
Caregivers' burden (score)	57.9 $\pm$ 9.1

NYHA = New York Heart Association, Lf = low-frequency, Hf = high-frequency, QoL = quality of life.

**Table 2**  
Multiple logistic regression analysis of the clinical and psychosocial variables for increased sympathetic nerve activity in patients with heart failure.

Variables	β-coefficient	P-value
Age of patients	0.14	0.513
Duration of heart failure	-0.34	0.455
Hospitalization due to heart failure	-0.24	0.842
NYHA classification	-0.06	0.841
Depression of patients	0.005	0.956
Depression of family caregivers	-0.266	0.09
QoL of patients	0.021	0.319
QoL of family caregivers	0.001	0.983
Self-care behavior of patients	0.053	0.218
Caregivers' burden	0.025	0.475

CI = confidence interval, NYHA = New York Heart Association, QoL = quality of life.

**Table 3**  
Multiple logistic regression analysis of the clinical and psychosocial variables for decreased parasympathetic nerve activity in patients with heart failure.

Variables	β-coefficient	P-value
Age of patients	0.034	0.299
Duration of heart failure	-0.079	0.252
Hospitalization due to heart failure	-0.038	0.832
NYHA classification	-0.307	0.502
Depression of patients	0.044	0.746
Depression of family caregivers	0.309	0.039
QoL of patients	0.032	0.325
QoL of family caregivers	0.001	0.986
Self-care behavior of patients	-0.029	0.047
Caregivers' burden	0.038	0.655

CI = confidence interval, NYHA = New York Heart Association, QoL = quality of life.

consists of maintaining self-care for physical and psychological stability and self-monitoring possible signs and symptoms of worsening.<sup>[18]</sup> Adequate self-care can help maintain a stable condition in patients by ensuring consistent treatment and enabling appropriate responses before HF aggravation occurs. The present study revealed that inadequate self-care behavior in patients with HF is related to parasympathetic withdrawal, which is associated with poor prognosis. Efforts to improve self-care behavior in patients might ultimately contribute to better clinical outcomes.

This study identified family caregiver depression as a significant factor influencing HRV in HF patients. As the world's population ages, there is an increasing prevalence of chronic long-term conditions including HF, which currently have no cure but can be managed. Aging patients with HF often face challenges in independent self-management due to cognitive or functional decline, emphasizing their significant dependence on family caregivers.<sup>[19]</sup> Our findings suggest that managing not only patients' but also their family caregivers' psychosocial factors can lead to better clinical outcomes in HF patients.

This study has several limitations. First, the duration of the pulse wave analyzer used to assess HRV was relatively short. While longer monitoring periods may offer superior data, there is limited research on the stability of long-term HRV measures from 24-hour ambulatory monitoring.<sup>[20]</sup> In clinical settings, short-term HRV measurement may be more useful and easily accessible. Second, as this was a cross-sectional and observational study, the clinical outcomes and effects of interventional treatment targeting psychosocial factors were not evaluated. The current findings provide evidence that psychosocial factors may be related to clinical outcomes in patients with HF.

**Table 4**  
Multiple logistic regression analysis of the clinical and psychosocial variables for increased autonomic nerve balance in patients with heart failure.

Variables	β-coefficient	P-value
Age of patients	0.004	0.15
Duration of heart failure	-0.007	0.164
Hospitalization due to heart failure	-0.008	0.551
NYHA classification	-0.058	0.109
Depression of patients	0.007	0.489
Depression of family caregivers	-0.002	0.837
QoL of patients	0.002	0.444
QoL of family caregivers	-0.001	0.835
Self-care behavior of patients	-0.007	0.154
Caregivers' burden	0.004	0.352

CI = confidence interval, NYHA = New York Heart Association, QoL = quality of life.

Specifically, some psychosocial factors in this study were related to HRV, which is associated with a poor prognosis. Further studies are needed to demonstrate the clinical outcomes and beneficial effects of interventional treatments targeting psychosocial factors on cardiovascular outcomes. Third, while some past research has investigated the link between family caregiver and patient psychosocial factors, they have not consistently shown clear connections. In the present study, we enrolled family caregivers exceeding 18 years of age and who accompanied patients to the clinic as primary caregivers. The highly selective study population may have affected the results of the present study. Families in this study demonstrated relatively strong bonds, which may have facilitated the impact of family caregiver psychosocial factors on patients with HF as compared to other family types. Considering the diversity of the family types, further studies are necessary to apply these findings in clinical practice. Given the diversity of family types shaped by social, economic, cultural and individual factors, understanding these variations and the distinct roles of family caregivers within each type is crucial. This deeper insight would inform further exploration of how family caregivers' psychosocial factors impact patients with HF. Fourth, specific trends of psychosocial factors in the study population may have influenced the study results. While participants reported relatively high QoL scores, patients' self-care scores indicated inadequate self-management, and caregivers' burden scores revealed moderate to severe levels of burden. This may be attributed to the relatively older age of the enrolled patients (72 ± 13 year-old). Further studies are needed to explore potential biases that may have affected the results of the present study.

In conclusion, psychosocial factors, including depression in family caregivers and the self-care behavior of patients, may affect HRV in patients with HF. Clinicians should be aware of the importance of psychosocial factors for a better prognosis in both patients and their family caregivers.

**Author contributions**

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