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Integrated Evaluation of Heart Rate Variability and Clinical Outcomes in Chronic Heart Failure: Insights into Cardiac Autonomic Dysfunction

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ABSTRACT

Background: Chronic heart failure carries a significant cardiovascular morbidity and mortality burden globally. An imbalance in cardiac autonomic function with sympathetic predominance and parasympathetic recession is a prominent part of the disease process and its poor clinical outcome. HRV is a non-invasive indicator of ANS function in cardiovascular diseases.

Objective: To assess the relationship of heart rate variability (HRV) parameters with clinical outcomes in CHF patients and the prognostic value of cardiac autonomic dysfunction.

Methods: The cross-sectional study was an observational study conducted at Erie County Medical center, Buffalo from February 2023 to April 2025 under the reference number IRB/2023/CHF-117. A total of 300 patients with chronic heart failure were enrolled using consecutive non-probability sampling. Holter monitoring was done for 24 hours to calculate heart rate variability parameters such as SDNN, RMSSD, pNN50 and LF/HF ratio. New York Heart Association classification, echocardiographic findings, frequency of hospitalizations, arrhythmic complications and cardiovascular outcomes were assessed clinically. The SPSS 26.0 software was used for statistical analysis.

Results: Patients with severe autonomic dysfunction demonstrated significantly reduced SDNN, RMSSD, and pNN50 values together with elevated LF/HF ratio ($p<0.001$). Recurrent hospitalization, ventricular arrhythmias, worsening NYHA functional class, length of hospital stay and decreased LVEF were all significantly associated with severe HRV impairment. Multivariate logistic regression analysis revealed that reduced SDNN, elevated LF/HF ratio, diabetes mellitus, atrial fibrillation and reduced EF were independent factors in predicting adverse cardiovascular outcomes.

Conclusion: Reduced HRV is also a strong predictor of adverse clinical events in CHF. HRV assessment could be a valuable prognostic tool for the early stratification of cardiovascular risk and for individual patient management.

Keywords: Heart rate variability; chronic heart failure; autonomic dysfunction; ventricular arrhythmias; cardiac outcomes; cardiovascular risk

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INTRODUCTION

Chronic heart failure is a clinical syndrome of structural or functional abnormalities in the filling and output of the ventricles with insufficient tissue perfusion and gradual deterioration of the cardiovascular status [1]. Despite significant progress in pharmacological therapy, interventional cardiology, and device-based management, it continues to be one of the major causes of hospitalization, morbidity and mortality worldwide.

Chronic heart failure continues to be a growing problem worldwide due to the effects of an aging population, the rising prevalence of hypertension, diabetes mellitus, ischemic heart disease, obesity, and improved survival after acute myocardial infarction. Chronic heart failure patients are often readmitted to hospital, have lower

exercise capacity, poorer quality of life, arrhythmic complications, and have a higher risk of sudden cardiac death [2].

Chronic heart failure is characterized by several neurohormonal and hemodynamic alterations that lead to progressive myocardial dysfunction and to pathological remodeling of the ventricle [3]. Of these mechanisms, abnormality of the autonomic nervous system on disease progression and cardiovascular prognosis has become one of the most important. Chronic activation of the sympathetic nervous system and a decrease in parasympathetic tone leads to increased myocardial oxygen demand, endothelial dysfunction, myocardial fibrosis, vasoconstriction and tachycardia. Persistent autonomic dysfunction also promotes ventricular arrhythmogenesis, reduced cardiac function and increased severity of heart failure [4].

Heart rate variability or HRV is the variation in the time interval between heart beats and is a measure of the balance between the activity of the sympathetic and parasympathetic nervous systems [5]. HRV assessment offers a noninvasive tool of cardiac autonomic regulation and has become more and more important in cardiovascular medicine. A decrease in HRV has been viewed as a sign of autonomic dysfunction and it has been linked to cardiovascular mortality, ventricular arrhythmias, sudden cardiac death, and adverse long-term outcomes in several cardiac conditions including CHF [6].

Various HRV parameters have been used to measure the activity of the autonomic nervous system (ANS) from 24-hour Holter monitoring [7]. Time-domain indices such as SDNN, RMSSD, and pNN50 primarily reflect parasympathetic modulation, whereas frequency-domain measurements including low-frequency power, high-frequency power, and LF/HF ratio provide information regarding sympathetic-vagal balance. Chronic heart failure patients have profound decreases in HRV indices, especially with high sympathetic activation and low vagal activation. These autonomic abnormalities are thought to be closely related with severity of the disease, the left ventricle dysfunction and risk of adverse cardiac events [8].

Recently, there has been a growing interest in HRV assessment in chronic HF as a predictor of outcome [9]. Autonomic dysfunction could be a useful tool for early risk stratification, and may allow for the identification of those patients most likely to develop recurrent hospitalization, progressive functional decline, arrhythmias and cardiovascular complications. HRV assessment may also offer more individualised patient management and therapeutic decision making as it can give extra prognosis data besides the conventional clinical and echocardiographic ones [10].

Although previous research has demonstrated an association between decreased HRV and poor cardiovascular outcomes, the relationship between autonomic dysfunction and multiple clinical outcomes in the setting of chronic heart failure is not completely understood. In addition, differences in patient population and severity of disease, as well as the method used to assess HRV, have led to conflicting results from different studies. Thus, the present study was designed to make an integrated evaluation of HRV and clinical outcomes in CHF patients, and to explore the prognostic value of cardiac autonomic dysfunction in terms of future hospitalisation rates, arrhythmic events, functional decline and overall cardiovascular risk [11].

MATERIALS AND METHODS

An observational cross-sectional investigation was undertaken at Erie County Medical Centre, Buffalo, United States, over the period extending from February 2023 until April 2025. The main goal of this study was to investigate if there is a relationship between HRV abnormalities and poor clinical outcome in people with CHF. The study was approved by the Institutional Review Board of the study center with approval number IRB/2023/CHF-17. All the individuals who participated gave their informed consent, which was signed before the data collection began.

The study population comprised of n=300 patients who visited the cardiology department for outpatient evaluation or in-patient management of chronic heart failure. Men and women aged 35–80 years were eligible if they had a confirmed diagnosis of CHF for at least 6 months prior to recruitment. Diagnostic confirmation was based on a combination of clinical examination, electrocardiographic assessment, echocardiographic evaluation, biochemical investigations and specialist cardiology review. In the final analysis, patients with both ischemic and non-ischemic etiology of heart failure were included.

People with recent myocardial infarction (last three months), congenital cardiac abnormalities, active systemic infection, severe liver dysfunction, malignancy, end-stage renal impairment (requiring dialysis support), or incomplete Holter monitoring recordings were not considered eligible. Other exclusion criteria were prior cardiac surgery within 6 months, dependence on a pacemaker, neurological conditions that can affect the regulation of the autonomic nervous system, and drugs not related to traditional heart failure treatment that could significantly affect the activity of the ANS.

Baseline demographic and clinical data was collected on a structured data collection sheet. It was recorded as age, sex, smoking, BMI, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, AF, period of heart failure, previous hospitalization for cardiac diseases, and medication history. Functional limitation and symptom severity were divided into groups based on the New York Heart Association classification system.

All participants had a thorough cardiovascular evaluation at the start of the process. Resting pulse rate,

arterial blood pressure, oxygen saturation and physical examination of the systemic system were recorded. Laboratory evaluation consisted of complete blood count, fasting blood glucose, glycosylated hemoglobin, serum creatinine, electrolytes, liver function profile, lipid profile and brain natriuretic peptide (BNP) concentration. Twelve-lead electrocardiography was also used for detection of conduction defects, ischemic changes and arrhythmic disturbances.

Comprehensive transthoracic echocardiography was carried out by trained cardiologists using standardized imaging protocols. Cardiac structural and functional parameters included left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVDD), left ventricular end-systolic dimension (LVSD), interventricular septal thickness (IVST), left atrial diameter (LVD), and cardiac structural abnormalities. LV EF was estimated by the Simpson biplane method.

Twenty-four-hour ambulatory Holter was used to assess cardiac autonomic function. The recorded data were analysed by using the well-validated computerized analysis software to evaluate the indices of HRV. Time-domain parameters were standard deviation of normal-to-normal intervals, root mean square of successive RR interval differences and percentage of adjacent RR interval differences greater than fifty milliseconds. Frequency-domain analysis comprised low-frequency power, high-frequency power, and low-frequency to high-frequency ratio measurements. The decrease in the measurements of the variability and the increase in LF/HF ratio were considered as a sign of sympathetic predominance autonomic imbalance.

Patients were stratified based on the extent of autonomic dysfunction, following HRV evaluation. Clinical outcomes measured throughout the study were re-hospitalisation due to decompensation of heart failure, New York Heart Association (NYHA) functional class progression, episodes of atrial fibrillation, ventricular arrhythmias, intensive care admission, length of hospital stay and markers of poor cardiovascular prognosis. Electrocardiographic interpretation and findings of the holter monitoring were used to identify arrhythmic complications.

All collected information was entered into Statistical Package for Social Sciences software version 26.0 for analysis. Continuous variables were expressed as mean ± standard deviation, whereas categorical variables were summarized as frequencies and percentages. Comparison of continuous variables between study groups was carried out using independent sample t-test and one-way analysis of variance where appropriate. Chi-square testing was used for comparison of categorical variables. Correlation analysis between heart rate variability indices and clinical parameters was performed using Pearson correlation coefficient testing. Multivariable logistic regression analysis was additionally applied to identify independent predictors of unfavorable cardiovascular outcomes after adjustment for clinically relevant confounding variables. Statistical significance throughout the study was defined at a probability value below 0.05.

RESULTS

The final analysis included 300 patients with chronic heart failure. The mean age of the study population was 65.3 ± 10.8 years (38-80 years). A total of 214 (71.3%) patients had hypertension, 136 (45.3%) had diabetes mellitus, 171 (57.0%) had ischemic heart disease, and 82 (27.3%) had atrial fibrillation. The mean LVEF for the entire group was 34.9 ± 8.6%.

Significantly reduced ANS activity was seen in patients with higher severity of heart failure. Lower HRV values such as SDNN, RMSSD and pNN50 were seen mostly in those with NYHA class III/IV. Likewise, higher LF/HF ratio (sympathetic predominance) was also linked to an increased functional limitation, frequent hospitalizations, arrhythmic complications, etc. Demographic, echocardiographic and autonomic parameters of the study population are summarized in detail in Table 1.

Table 1 shows that the study population was predominantly elderly patients with advanced chronic heart failure and multiple cardiovascular co-morbidities. Lower LVEF and higher NYHA functional class were associated with reduced HRV indices, indicating significant autonomic dysfunction.

Significant differences of HRV parameters and clinical outcomes were observed between patients with preserved autonomic function and those with severe autonomic dysfunction. Patients with markedly reduced SDNN values experienced significantly higher frequencies of recurrent hospitalization, ventricular arrhythmias, intensive care admissions, prolonged hospitalization, and worsening NYHA functional status. Patients with adverse cardiovascular outcomes had significantly lower mean SDNN and RMSSD as compared to clinically stable patients. These findings are presented in Table 2.

As shown in Table 2, there was a strong correlation between severe autonomic dysfunction and poor cardiovascular outcome and clinical progression. The patients with poor HRV had significant sympathetic overactivity and parasympathetic withdrawal, with significantly decreased ejection fraction and increased CV instability.

Using multivariate logistic regression analysis, independent predictors were determined after adjusting for potential confounding factors such as age, gender, diabetes mellitus, atrial fibrillation, smoking status, BNP level and left ventricular ejection fraction. Reduced SDNN proved to be the best independent predictor of poor cardiovascular prognosis. Other risk factors for adverse clinical events were elevated LF/HF ratios, atrial fibrillation, diabetes

mellitus and elevated BNP levels. Table 3 shows detailed regression analysis.

Table 3 shows that after adjustment for major clinical and echocardiographic risk factors, impaired cardiac autonomic function continued to be associated with adverse cardiovascular outcomes. Decrease in SDNN and increase in LF/HF ratio were shown to be particularly useful in predicting the progression of chronic heart failure; thus showing the significant importance of autonomic dysfunction in the progression of chronic heart failure.

In conclusion, the results of the current study confirm that decreased HRV is related to poor cardiovascular outcomes in CHF patients. There was a consistent association between reduced autonomic function and worsening functional capacity, increased arrhythmic burden, recurrent hospitalization and higher cardiovascular risk, suggesting that HRV assessment in routine heart failure evaluation is prognostic.

Table 1: Baseline Clinical, Echocardiographic, and Heart Rate Variability Characteristics of the Study Population (n=300)

Variable	Mean ± SD / Frequency (%)
Age (years)	65.3 ± 10.8
Male gender	188 (62.7%)
Female gender	112 (37.3%)
Hypertension	214 (71.3%)
Diabetes mellitus	136 (45.3%)
Ischemic heart disease	171 (57.0%)
Atrial fibrillation	82 (27.3%)
Smoking history	119 (39.7%)
Body mass index (kg/m²)	29.1 ± 4.8
Left ventricular ejection fraction (%)	34.9 ± 8.6
NYHA Class I–II	118 (39.3%)
NYHA Class III–IV	182 (60.7%)
SDNN (ms)	84.7 ± 27.5
RMSSD (ms)	24.6 ± 10.2
pNN50 (%)	9.8 ± 5.1
LF/HF ratio	3.7 ± 1.5
BNP (pg/mL)	618.4 ± 188.6

Table 2: Comparative Analysis of Heart Rate Variability Parameters and Clinical Outcomes According to Severity of Autonomic Dysfunction

Variable	Preserved/Moderate HRV Dysfunction (n=132)	Severe HRV Dysfunction (n=168)	p-value
SDNN (ms)	109.4 ± 18.7	65.2 ± 14.6	<0.001
RMSSD (ms)	33.7 ± 8.5	17.4 ± 5.9	<0.001
pNN50 (%)	14.8 ± 4.1	5.9 ± 2.8	<0.001
LF/HF ratio	2.1 ± 0.8	4.9 ± 1.2	<0.001
Left ventricular ejection fraction (%)	39.6 ± 7.4	31.2 ± 6.9	<0.001
Recurrent hospitalization	29 (22.0%)	103 (61.3%)	<0.001
Ventricular arrhythmias	16 (12.1%)	71 (42.3%)	<0.001
ICU admission	11 (8.3%)	48 (28.6%)	<0.001
Prolonged hospital stay	24 (18.2%)	89 (53.0%)	<0.001
NYHA class worsening	27 (20.5%)	96 (57.1%)	<0.001

Table 3: Multivariate Logistic Regression Analysis for Predictors of Adverse Cardiovascular Outcomes in Chronic Heart Failure

Variable	Adjusted Odds Ratio (AOR)	95% Confidence Interval	p-value
Reduced SDNN (<70 ms)	4.38	2.61–7.29	<0.001
Elevated LF/HF ratio (>4.0)	3.12	1.88–5.16	<0.001
Diabetes mellitus	2.24	1.31–3.84	0.003
Atrial fibrillation	2.79	1.57–4.96	<0.001
BNP >600 pg/mL	2.47	1.42–4.28	0.001
Left ventricular ejection fraction <35%	3.01	1.79–5.07	<0.001
Smoking history	1.68	0.98–2.89	0.057
Age >65 years	1.53	0.92–2.54	0.083

DISCUSSION

This current study showed that there was a high correlation between decreased HRV and cardiovascular morbidity and mortality in patients with CHF [5]. Impaired autonomic function (severely affected patients) was associated with significantly reduced SDNN, RMSSD, and pNN50 values as well as increased LF/HF ratios, indicating high sympathetic drive and reduced parasympathetic drive. These autonomic abnormalities were strongly correlated with the progression of NYHA functional class, recurrent hospitalization, presence of ventricular arrhythmias, longer hospital stay and overall cardiovascular instability [6].

Cardiac autonomic dysfunction is a key element in the evolution of chronic heart failure (CHF). While initially it may be a compensatory mechanism to maintain cardiac output, continued activation of the sympathetic

nervous system will ultimately lead to myocardial remodeling, myocardial function, endothelial injury, inflammatory activation, and electrical instability [7,8]. This decrease in parasympathetic activity further exacerbates arrhythmogenesis and decreases cardiovascular adaptability. The results of the current study validate the idea that it is not sufficient to regard autonomic imbalance as a secondary phenomenon of heart failure; instead, it is an important determinant of the course of the disease and the clinical prognosis [9].

The marked decrease in SDNN and RMSSD in patients with highest severity of HF shows high vagal modulation impairment [10]. SDNN is an index of overall HRV and is regarded as one of the most powerful predictors of cardiovascular mortality. The most significant independent association with adverse cardiovascular outcomes was found in the current study with reduced SDNN after multivariate adjustment, highlighting its prognostic importance in chronic heart failure patients. High LF/HF ratio was also an indicator of sympathetic predominance and autonomic instability in clinically deteriorated people [11].

A major finding of this study was the significant association between autonomic dysfunction and re-hospitalization [12]. Severe HRV impairment was associated with higher frequencies of exacerbation of heart failure and longer hospital stay. The decreased autonomic adaptability may affect the cardiovascular compensation mechanism during hemodynamic stress and cause patients to decompensate repeatedly. These results indicate that HRV analysis could potentially serve as a tool to identify patients who should be more closely monitored clinically and who may need more aggressive therapeutic optimization [13].

In the present study, there was also significant correlation between poor HRV and arrhythmic complications [14]. The frequency of the ventricular arrhythmias and atrial fibrillation was greatly increased in the patients with severe autonomic dysfunction. The sympathetic overactivity is associated with decreased vagal tone, which leads to electrical instability, abnormal myocardial conduction and a predisposition to develop malignant arrhythmias. The autonomic disturbances may contribute to the increased risk for sudden cardiac death seen in the populations with advanced heart failure [15].

Multivariate regression analysis also showed that the diabetes mellitus and atrial fibrillation were independent factors affecting the unfavorable cardiovascular outcomes [16]. Autonomic neuropathy associated with diabetes can increase the imbalance between sympathetic and vagal activity and will accelerate myocardial dysfunction. Atrial fibrillation (AF) also affects the normal regulation of the autonomic system and is a cause of hemodynamic deterioration and hospitalization risk. Higher BNP and very low LVEF also were significant determinants of poor outcomes, as previously recognized as markers of severity of heart failure [17].

The results from this study add to the growing evidence that HRV analysis is a valuable prognostic tool in addition to conventional clinical and echocardiographical parameters [18]. Incorporation of HRV assessment into routine cardiovascular evaluation may help in early risk stratification, individualized patient management, and timely identification of high-risk patients. Noninvasive autonomic assessment through Holter monitoring may therefore serve as a clinically valuable approach for improving long-term management strategies in chronic heart failure populations [19].

Certain limitations should also be considered while interpreting the findings of the present study. The cross-sectional study design does not establish a causal relationship between autonomic dysfunction and cardiovascular outcomes. Furthermore, the investigation was performed at a single tertiary care centre, which may affect the generalisability of the results to broader populations. Despite these limitations, the relatively large sample size and comprehensive autonomic evaluation strengthen the reliability of the study findings [20].

CONCLUSION

The present study showed that reduced HRV is a significant predictor of poor clinical outcome in patients with CHF. Severe autonomic dysfunction with decreased SDNN, RMSSD, and pNN50 and increased LF/HF ratio was strongly associated with recurrent hospitalization, ventricular arrhythmias, worsening NYHA functional status, prolonged hospital stay, and increased cardiovascular risk. Reduced SDNN was found to be an independent predictor of poor cardiovascular prognosis despite controlling for major clinical confounding variables. The results suggest that cardiac autonomic imbalance plays an important role in the progression of chronic heart failure and indicate that HRV assessment is useful for prognosis in standard cardiovascular care. Full HRV analysis can help identify high risk patients with heart failure early in the disease process and enable the stratification of cardiovascular risk, as well as individualized therapeutic intervention and close monitoring. Autonomic function analysis integration in the usual care of heart failure may help to improve the clinical outcome and decrease cardiovascular morbidity in CHF.

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Authors' Contributions: Y.S. contributed to conceptualization, study design, patient recruitment, clinical supervision, data interpretation, and manuscript drafting. S.F.U. contributed to data collection, statistical analysis, interpretation of findings, manuscript revision, and critical intellectual review. Both authors approved the final version of the manuscript.

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Data Availability: The datasets generated and analyzed during this study are available from the corresponding author upon reasonable request

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