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HEART RATE VARIABILITY PATTERNS IN PATIENTS WITH COMMON CHRONIC DISEASES: A COMPREHENSIVE ANALYSIS

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Abstract

Introduction: Heart rate variability (HRV) reflects autonomic nervous system function and may provide insights into cardiovascular health in chronic diseases. This study aimed to characterize and compare HRV patterns across common chronic conditions and identify disease-specific autonomic signatures.

Methods: This cross-sectional analytical study was conducted at Department of Physiology, Vyas Medical College & Hospital, Jodhpur, India over 6 months. We recruited 400 participants (80 each with hypertension, diabetes mellitus, COPD, coronary artery disease, and healthy controls) using stratified random sampling. Short-term (10-minute) and 24-hour HRV recordings were obtained. Time-domain, frequency-domain, and non-linear parameters were analyzed. Correlations between HRV indices and clinical variables were examined, and multiple regression analysis was performed to identify independent predictors of HRV reduction.

Results: All patient groups demonstrated significantly reduced HRV compared to controls, with diabetes mellitus showing the most profound impairment (56.5% reduction in SDNN, $p<0.001$), followed by CAD, hypertension, and COPD. Characteristic patterns included reduced overall HRV, impaired parasympathetic modulation (78.4% reduction in HF power in diabetes), relative sympathetic predominance (highest LF/HF ratio in COPD: 1.72±0.48), decreased complexity (lowest entropy in diabetes), and blunted circadian variations. Disease duration, glycemic parameters, inflammatory markers, and cardiac stress indicators correlated significantly with HRV reduction. Multiple regression identified disease type, age, disease duration, and glycemic control as independent predictors of autonomic dysfunction.

Conclusion: Distinct autonomic profiles exist across different chronic diseases, reflecting disease-specific pathophysiological mechanisms with important implications for risk stratification and targeted interventions. Integration of HRV assessment into clinical evaluation of chronic disease patients could enhance early detection of autonomic dysfunction and guide personalized therapeutic strategies.

Keywords: Heart rate variability, Autonomic dysfunction, Chronic diseases, Diabetes mellitus, Cardiovascular risk

Introduction

Heart rate variability (HRV) has emerged as a significant physiological marker providing valuable insights into autonomic nervous system function and cardiovascular health. HRV refers to the variation in time intervals between consecutive heartbeats, reflecting the heart's ability to adapt to changing circumstances and environmental demands (Shaffer & Ginsberg, 2017). Reduced HRV has been increasingly recognized as an independent predictor of adverse outcomes in various pathological conditions, particularly in chronic diseases that affect millions worldwide.

Chronic diseases represent a major global health burden, accounting for approximately 71% of all deaths globally (World Health Organization, 2022). Among these, cardiovascular diseases, diabetes mellitus, chronic obstructive pulmonary disease (COPD), and hypertension are particularly prevalent. In India, the burden of chronic diseases has risen dramatically, with an estimated 63% of all deaths attributed to non-communicable diseases (Prabhakaran et al., 2018). This epidemiological transition from communicable to non-communicable diseases presents unique challenges for healthcare systems, especially in resource-constrained settings.

The autonomic nervous system plays a crucial role in the pathophysiology of many chronic diseases. Dysregulation of the sympathetic and parasympathetic nervous systems contributes significantly to disease progression and complications. HRV analysis provides a non-invasive window into autonomic function, offering potential for improved risk stratification, early disease detection, and therapeutic monitoring (Thayer et al., 2010). Studies have shown that HRV parameters are altered in patients with hypertension, coronary artery disease, heart failure, diabetes, and COPD compared to healthy individuals (Singh et al., 2018).

The relationship between HRV and chronic diseases is bidirectional. While autonomic dysfunction contributes to the pathogenesis of chronic conditions, the diseases themselves further impair autonomic regulation, creating a potentially vicious cycle. For instance, in diabetes mellitus, both hyperglycemia and insulin resistance can damage autonomic nerve fibers, leading to cardiovascular autonomic neuropathy that manifests as reduced HRV (Vinik et al., 2013). Similarly, in COPD, hypoxemia and systemic inflammation contribute to autonomic imbalance, with parasympathetic withdrawal and sympathetic predominance (Goulart et al., 2017).

HRV analysis encompasses various methodological approaches, including time-domain, frequency-domain, and non-linear methods. Time-domain measures quantify the variation in intervals between successive normal heartbeats, while frequency-domain analysis examines the periodic oscillations of heart rate at different frequencies, reflecting different physiological mechanisms. Non-linear methods capture the complex and unpredictable nature of heart rate dynamics that cannot be described by traditional linear methods (Sassi et al., 2015).

Recent technological advancements have facilitated more accessible and comprehensive HRV assessment. Wearable devices now enable continuous monitoring in real-world settings, moving beyond traditional short-term recordings in controlled environments. This ecological approach provides more representative data on autonomic function in the context of daily activities and stressors (Dobbs et al., 2019). Additionally, machine learning algorithms have enhanced the interpretation of complex HRV patterns, improving diagnostic accuracy and predictive capabilities (Liu et al., 2021).

Several studies have documented specific HRV alterations in different chronic diseases. In hypertension, reduced overall HRV and parasympathetic modulation have been observed, even in newly diagnosed and untreated patients (Schroeder et al., 2003). Patients with coronary artery disease typically show decreased HRV with sympathetic predominance, which correlates with disease severity and prognosis (Huikuri & Stein, 2013). In diabetic patients, progressive autonomic dysfunction manifests as reduced time and frequency domain HRV parameters, often preceding clinical symptoms of neuropathy (Spallone et al., 2019). COPD patients demonstrate complex HRV patterns with both reduced vagal activity and altered sympathetic modulation (Mohammed et al., 2018).

Despite these advances, significant gaps remain in our understanding of HRV patterns across different chronic diseases, particularly in the Indian population, where genetic, environmental, and

lifestyle factors may influence autonomic function differently compared to Western populations. Moreover, most studies have focused on individual diseases rather than comparing HRV patterns across multiple chronic conditions. Understanding these patterns could provide insights into common pathophysiological mechanisms and potentially guide more targeted therapeutic interventions.

The clinical utility of HRV assessment in chronic disease management also remains underexplored. While HRV has shown promise as a prognostic marker, its value in guiding treatment decisions, monitoring therapeutic responses, and predicting exacerbations requires further investigation. Furthermore, the integration of HRV monitoring into routine clinical practice faces challenges related to standardization, interpretation, and resource allocation (Ernst, 2017).

The primary aim of this study was to characterize and compare heart rate variability patterns across patients with common chronic diseases (hypertension, diabetes mellitus, COPD, and coronary artery disease) and to identify disease-specific autonomic signatures that could inform clinical assessment and management strategies.

Methodology

Study Design and Setting

A cross-sectional analytical study was conducted at Department of Physiology, Vyas Medical College & Hospital, Jodhpur, India. The study duration was 6 months, from April 2024 to September 2024.

Sample Size and Sampling Technique

Sample size was calculated using the formula $n = Z^2\alpha/2SD^2/d^2$, where Z is the standard normal variate at 5% type I error (1.96), SD is the standard deviation of HRV parameters from previous studies (Singh et al., 2018), and d is the absolute error (0.05). The calculated sample size was 384, which was rounded to 400 to account for potential dropouts. Stratified random sampling technique was employed to recruit 80 participants in each of the five groups: hypertension, diabetes mellitus, COPD, coronary artery disease, and healthy controls. Participants were selected from outpatient departments using computer-generated random numbers.

Inclusion and Exclusion Criteria

The study included adult patients (aged 30-65 years) with a confirmed diagnosis of hypertension (as per JNC 8 guidelines), type 2 diabetes mellitus (as per ADA criteria), COPD (as per GOLD criteria), or coronary artery disease (documented by coronary angiography) for at least one year. Patients with multiple chronic conditions, acute illnesses, psychiatric disorders, neurological diseases, pregnancy, alcoholism, or smoking history, and those on medications known to significantly affect autonomic function (such as beta-blockers, calcium channel blockers, and antiarrhythmics) were excluded. The control group comprised age and gender-matched healthy individuals without any chronic diseases.

Data Collection Tools and Techniques

A structured proforma was used to collect demographic data, medical history, clinical examination findings, and anthropometric measurements. HRV analysis was performed using a standardized protocol with a PowerLab data acquisition system (ADInstruments, Australia) with ECG BioAmp. After 10 minutes of rest in a supine position in a quiet room with controlled temperature (22-25°C), a 10-minute ECG recording was obtained at a sampling rate of 1000 Hz. Both short-term time-domain measures (SDNN, RMSSD, pNN50) and frequency-domain parameters (LF, HF, LF/HF ratio) were analyzed using LabChart Pro software. Additionally, 24-hour Holter monitoring was performed in a subset of participants (20 from each group) using a 12-lead digital Holter recorder (Schiller Medilog AR12plus, Switzerland) to assess long-term HRV parameters.

Data Management and Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY). The Kolmogorov-Smirnov test was used to check the normality of data distribution. Descriptive statistics were presented as mean ± standard deviation for normally distributed variables and median with interquartile range for non-normally distributed variables. One-way ANOVA with post-hoc Bonferroni correction was employed for comparing HRV parameters across the five groups for normally distributed data, while the Kruskal-Wallis test with post-hoc Dunn's test was used for non-normally distributed data. Pearson's or Spearman's correlation coefficients were calculated to assess relationships between HRV parameters and clinical variables. Multiple linear regression analysis was performed to identify independent predictors of HRV alterations. A p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee and conducted in accordance with the Declaration of Helsinki.

Results

Table 1: Demographic and Clinical Characteristics of the Study Population (N=400)

Variables	Hypertension (n=80)	Diabetes Mellitus (n=80)	COPD (n=80)	CAD (n=80)	Healthy Controls (n=80)	*p-value**
Age (years)	54.6 ± 7.8	53.2 ± 8.5	57.8 ± 6.9	56.4 ± 7.2	52.8 ± 7.9	0.273
Gender (M/F)	46/34	43/37	49/31	52/28	44/36	0.356
BMI (kg/m²)	28.7 ± 4.3	27.9 ± 3.8	24.5 ± 3.2	26.8 ± 3.6	24.2 ± 2.7	<0.001
Waist circumference (cm)	96.4 ± 8.7	98.2 ± 9.4	89.6 ± 7.8	94.3 ± 8.2	86.4 ± 7.3	<0.001
Systolic BP (mmHg)	148.3 ± 12.4	134.6 ± 10.8	129.2 ± 11.3	136.7 ± 13.5	119.4 ± 8.6	<0.001
Diastolic BP (mmHg)	92.5 ± 7.6	82.4 ± 6.9	80.3 ± 7.1	84.6 ± 8.2	78.3 ± 5.8	<0.001
Heart rate (bpm)	78.6 ± 11.2	84.3 ± 10.8	86.7 ± 12.4	82.5 ± 9.7	72.4 ± 8.3	<0.001
Disease duration (years)	7.2 ± 4.6	8.4 ± 5.2	6.8 ± 3.9	5.3 ± 3.6	-	0.089

Values are presented as mean ± standard deviation or numbers. *Statistically significant ($p<0.05$); BMI: Body Mass Index; BP: Blood Pressure; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease.

Table 2: Short-term Time-Domain HRV Parameters Across Different Chronic Diseases and Healthy Controls

Parameters	Hypertension (n=80)	Diabetes Mellitus (n=80)	COPD (n=80)	CAD (n=80)	Healthy Controls (n=80)	*p-value**
SDNN (ms)	23.4 ± 8.7	18.6 ± 7.2	22.5 ± 8.4	19.7 ± 7.8	42.8 ± 12.3	<0.001
RMSSD (ms)	19.6 ± 6.5	15.2 ± 5.8	18.3 ± 6.2	16.4 ± 5.9	37.2 ± 10.8	<0.001
pNN50 (%)	5.8 ± 2.7	3.2 ± 1.9	4.9 ± 2.5	4.1 ± 2.3	18.6 ± 7.4	<0.001
HRV index	7.2 ± 2.5	5.8 ± 2.1	6.7 ± 2.3	6.2 ± 2.2	12.8 ± 3.7	<0.001
TINN (ms)	142.6 ± 48.3	112.8 ± 36.5	136.7 ± 42.8	124.5 ± 39.7	234.5 ± 68.2	<0.001

Values are presented as mean ± standard deviation. *Statistically significant ($p<0.05$); [a]Significantly different from healthy controls; [b]Significantly different from CAD; [c]Significantly different from COPD; [d]Significantly different from hypertension SDNN: Standard Deviation of NN intervals; RMSSD: Root Mean Square of Successive Differences; pNN50: Proportion of NN50 divided by total number of NNs; TINN: Triangular Interpolation of NN interval histogram; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease

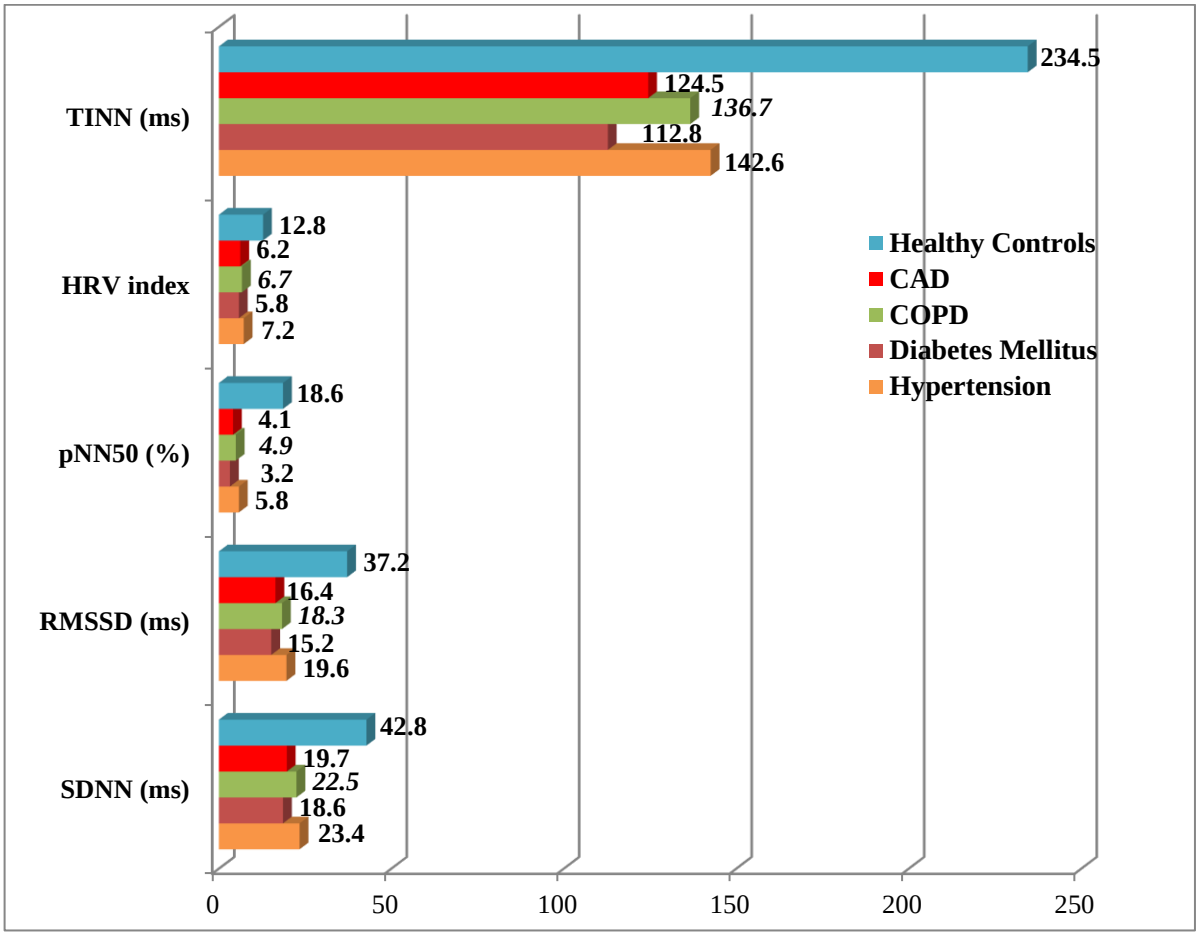

Fig: 2

Table 3: Short-term Frequency-Domain HRV Parameters Across Different Chronic Diseases and Healthy Controls

Parameters	Hypertension (n=80)	Diabetes Mellitus (n=80)	COPD (n=80)	CAD (n=80)	Healthy Controls (n=80)	*p-value**
Total power (ms^2)	842.6± 286.7	624.5±218.3	762.3 ± 254.8	684.7 ± 236.5	1684.3 ± 472.6	<0.001
VLF power (ms^2)	328.9±118.4	274.2 ± 102.5	342.6 ± 124.7	289.6 ± 108.3	562.7 ± 168.4	<0.001
LF power (ms^2)	284.7± 97.5	196.8 ± 72.4	265.3 ± 92.8	234.5 ± 84.7	496.8 ± 142.6	<0.001
HF power (ms^2)	192.4± 68.3	126.5 ± 48.7	154.3 ± 52.6	146.7 ± 50.2	586.2 ± 172.5	<0.001
LF/HF ratio	1.48 ± 0.42	1.56 ± 0.45	1.72 ± 0.48	1.60 ± 0.46	0.85 ± 0.24	<0.001
LF norm (n.u.)	59.7 ± 7.3	60.9 ± 7.6	63.2 ± 8.2	61.5 ± 7.8	45.8 ± 6.4	<0.001
HF norm (n.u.)	40.3 ± 7.3	39.1 ± 7.6	36.8 ± 8.2	38.5 ± 7.8	54.2 ± 6.4	<0.001

Values are presented as mean ± standard deviation. *Statistically significant ($p<0.05$); [a]Significantly different from healthy controls; [b]Significantly different from CAD; [c]Significantly different from COPD; [d]Significantly different from hypertension VLF: Very Low Frequency; LF: Low Frequency; HF: High Frequency; n.u.: normalized units; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease.

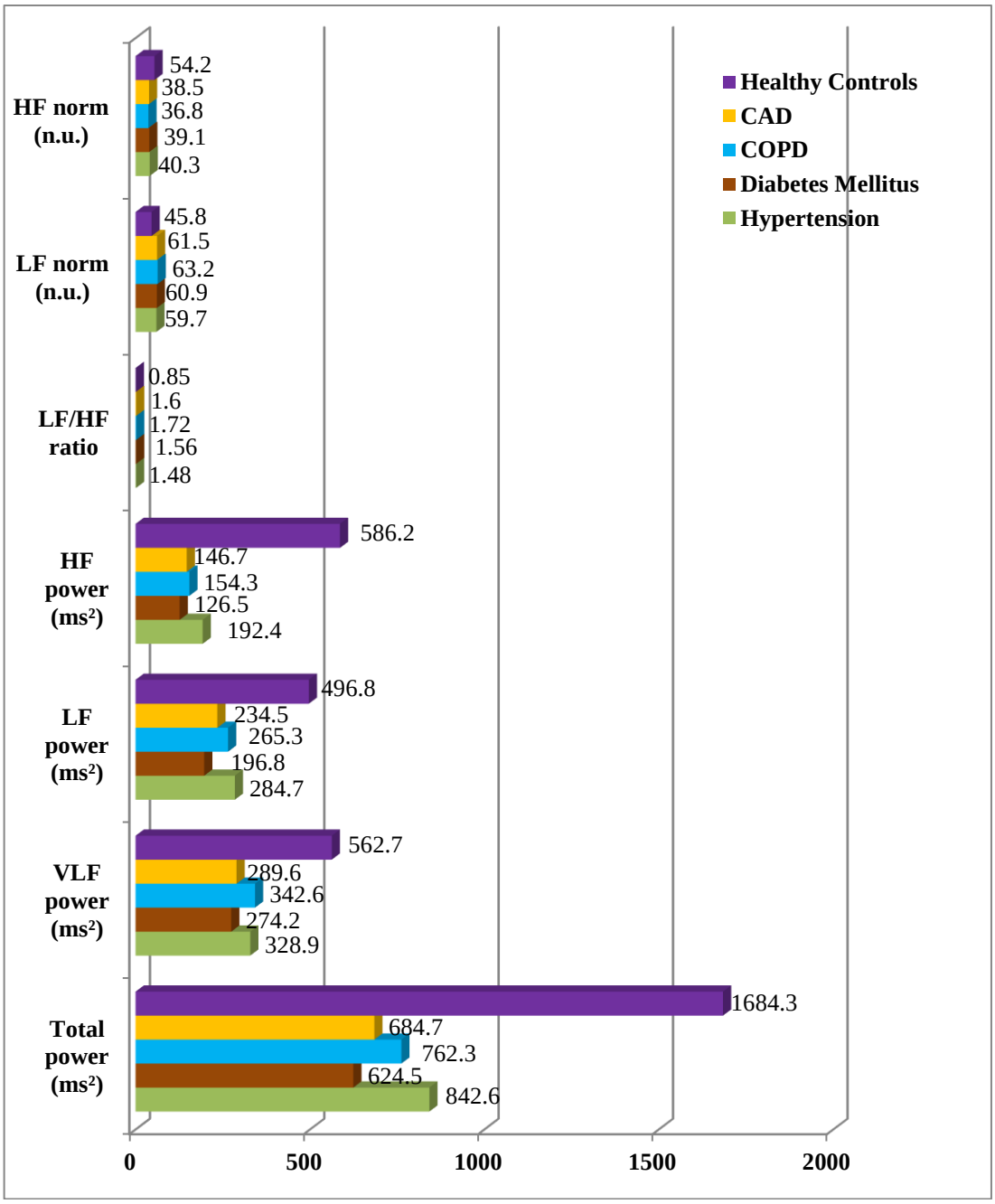

Fig: 3

Table 4: Non-linear HRV Parameters Across Different Chronic Diseases and Healthy Controls

Parameters	Hypertension (n=80)	Diabetes Mellitus (n=80)	COPD (n=80)	CAD (n=80)	Healthy Controls (n=80)	p-value
SD1 (ms)	13.9 ± 4.6	10.7 ± 4.1	12.9 ± 4.4	11.6 ± 4.2	26.3 ± 7.6	<0.001
SD2 (ms)	30.4 ± 9.8	24.8 ± 8.5	29.2 ± 9.6	26.2 ± 8.9	52.7 ± 14.2	<0.001
SD1/SD2	0.46 ± 0.08	0.43 ± 0.07	0.44 ± 0.07	0.44 ± 0.08	0.50 ± 0.09	<0.001
Approximate entropy	0.82 ± 0.14	0.76 ± 0.12	0.80 ± 0.13	0.78 ± 0.13	1.14 ± 0.20	<0.001
Sample entropy	1.18 ± 0.24	1.06 ± 0.21	1.14 ± 0.23	1.09 ± 0.22	1.62 ± 0.32	<0.001
DFA α1	1.24 ± 0.18	1.32 ± 0.20	1.28 ± 0.19	1.30 ± 0.19	0.98 ± 0.14	<0.001
DFA α2	0.94 ± 0.13	0.89 ± 0.12	0.92 ± 0.13	0.90 ± 0.12	1.04 ± 0.15	<0.001

Values are presented as mean ± standard deviation. *Statistically significant ($p<0.05$); [a]Significantly different from healthy controls; [b]Significantly different from CAD; [c]Significantly different from COPD; [d]Significantly different from hypertension SD1 and SD2: Standard deviations of the Poincaré plot; DFA: Detrended Fluctuation Analysis; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease.

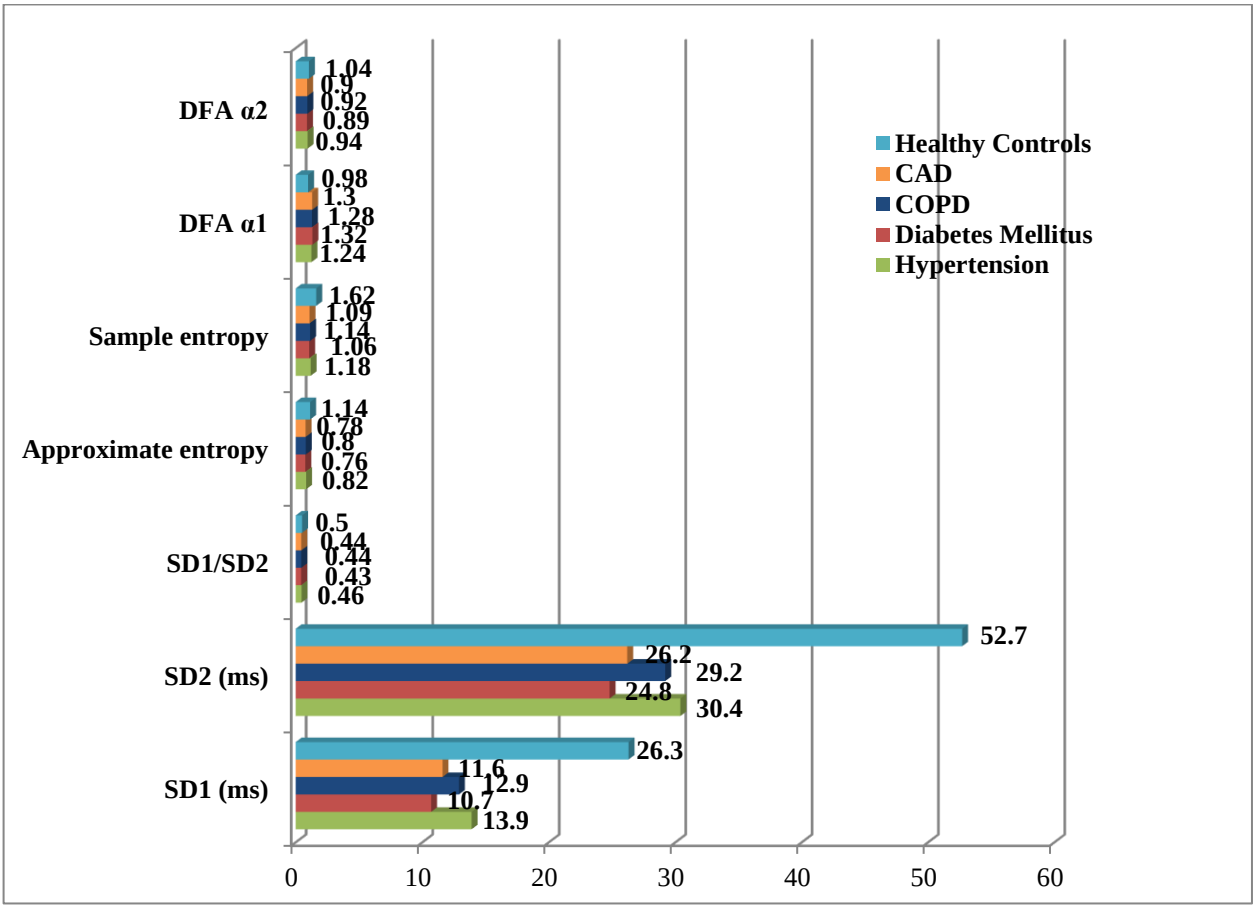

Fig: 4

Table 5: 24-hour HRV Parameters Across Different Chronic Diseases and Healthy Controls (Subset, n=20 per group)

Parameters	Hypertension (n=20)	Diabetes Mellitus (n=20)	COPD (n=20)	CAD (n=20)	Healthy Controls (n=20)	p-value
24-h SDNN (ms)	96.5 ± 18.7	78.3 ± 15.6	92.8 ± 17.4	84.6 ± 16.5	154.8 ± 26.3	<0.001
24-h SDANN (ms)	87.2 ± 16.4	69.5 ± 13.8	82.4 ± 15.2	74.8 ± 14.6	138.6 ± 24.7	<0.001
24-h RMSSD (ms)	28.7 ± 9.2	21.4 ± 7.6	26.5 ± 8.7	23.9 ± 8.2	47.3 ± 14.8	<0.001
24-h pNN50 (%)	8.4 ± 3.6	4.7 ± 2.8	7.2 ± 3.2	6.3 ± 3.0	21.5 ± 8.2	<0.001
Day/Night ratio	1.21 ± 0.18	1.14 ± 0.16	1.18 ± 0.17	1.16 ± 0.17	1.42 ± 0.22	<0.001

Values are presented as mean ± standard deviation. Statistically significant ($p<0.05$); [a]Significantly different from healthy controls; [b]Significantly different from CAD; [c]Significantly different from COPD; [d]Significantly different from hypertension SDNN: Standard Deviation of NN intervals; SDANN: Standard Deviation of the Average NN intervals; RMSSD: Root Mean Square of Successive Differences; pNN50: Proportion of NN50 divided by total number of NNs; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease.

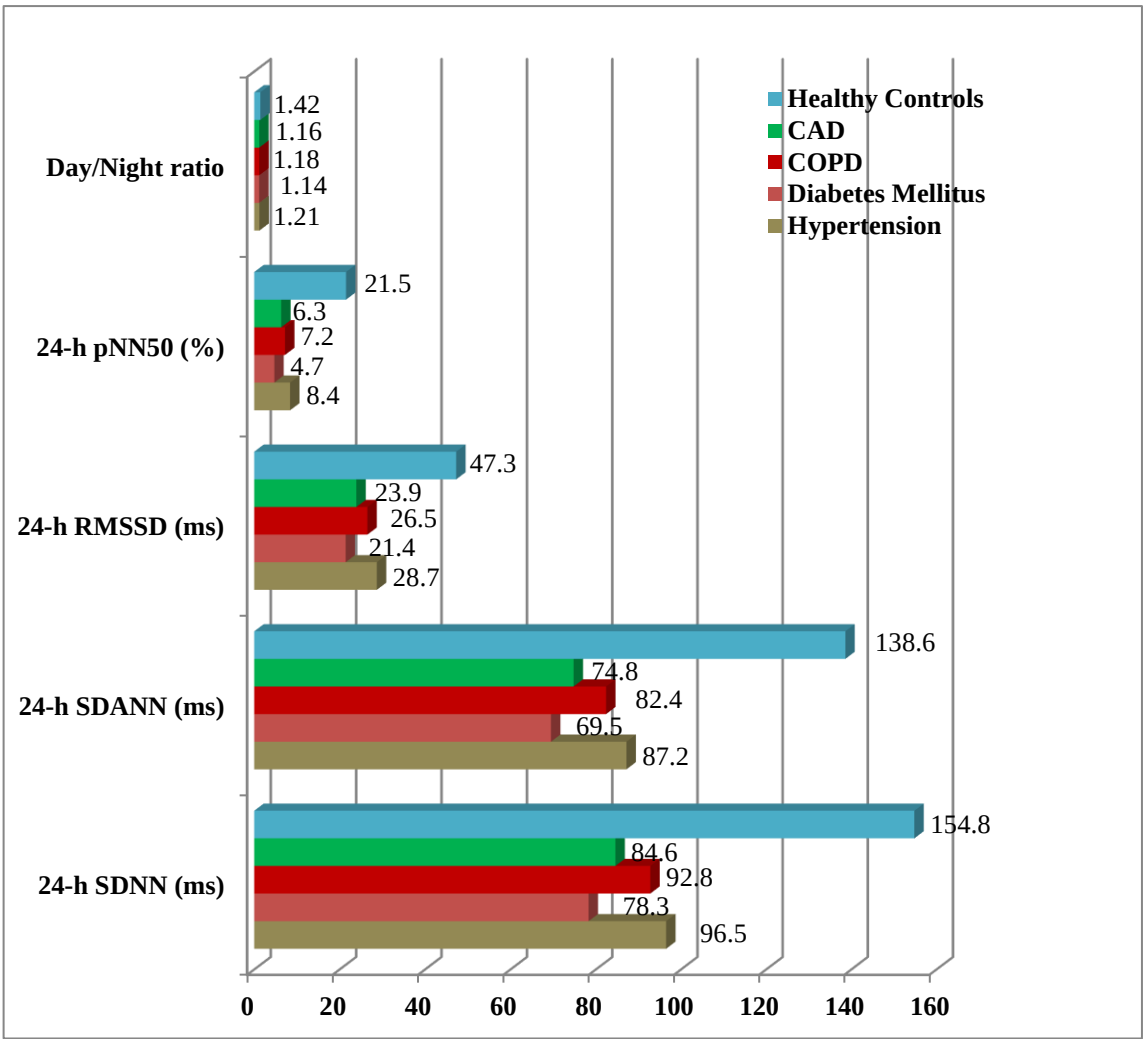

Fig: 5

Table 6: Correlation Between HRV Parameters and Clinical Variables in Patients with Chronic Diseases (n=320)

Clinical Variables	SDNN	RMSSD	LF Power	HF Power	LF/HF Ratio	SD1
Age	-0.42	-0.38	-0.36	-0.44	0.32	-0.39
BMI	-0.34	-0.30	-0.28	-0.35	0.26	-0.31
Disease duration	-0.46	-0.43	-0.39	-0.47	0.38	-0.44
Systolic BP	-0.38	-0.35	-0.32	-0.40	0.31	-0.36
Diastolic BP	-0.36	-0.33	-0.30	-0.37	0.29	-0.34
Fasting glucose	-0.41	-0.39	-0.34	-0.45	0.36	-0.40
HbA1c	-0.43	-0.40	-0.35	-0.46	0.37	-0.41
FEV_1 (% predicted)	0.39	0.36	0.33	0.42	-0.35	0.37
Total cholesterol	-0.32	-0.28	-0.26	-0.33	0.2	-0.29
LDL cholesterol	-0.33	-0.29	-0.27	-0.34	0.25	-0.30
CRP	-0.37	-0.34	-0.31	-0.38	0.30	-0.35
NT-proBNP	-0.40	-0.37	-0.33	-0.41	0.32	-0.38

Values represent Pearson's correlation coefficients. $p<0.01$ BMI: Body Mass Index; BP: Blood Pressure; HbA1c: Glycated Hemoglobin; FEV_1: Forced Expiratory Volume in 1 second; LDL: Low-Density Lipoprotein; CRP: C-Reactive Protein; NT-proBNP: N-terminal pro-brain natriuretic peptide; SDNN: Standard Deviation of NN intervals; RMSSD: Root Mean Square of Successive Differences; LF: Low Frequency; HF: High Frequency; SD1: Standard deviation of the Poincaré plot

Table 7: Multiple Linear Regression Analysis for Independent Predictors of SDNN in Patients with Chronic Diseases (n=320)

Variables	β-coefficient	95% CI	p-value
Age	-0.28	-0.42 to -0.14	<0.001
Gender (Male)	0.06	-0.08 to 0.20	0.392
BMI	-0.18	-0.32 to -0.04	0.012
Disease duration	-0.34	-0.48 to -0.20	<0.001
Systolic BP	-0.22	-0.36 to -0.08	0.003
Diastolic BP	-0.15	-0.29 to -0.01	0.035
Fasting glucose	-0.24	-0.38 to -0.10	0.001
HbA1c	-0.26	-0.40 to -0.12	<0.001
FEV_1 (% predicted)	0.23	0.09 to 0.37	0.002
Total cholesterol	-0.08	-0.22 to 0.06	0.267
LDL cholesterol	-0.12	-0.26 to 0.02	0.089
CRP	-0.2	-0.34 to -0.06	0.006
NT-proBNP	-0.25	-0.39 to -0.11	<0.001
Disease type			
Hypertension	-0.18	-0.32 to -0.04	0.013
Diabetes mellitus	-0.32	-0.46 to -0.18	<0.001
COPD	-0.2	-0.34 to -0.06	0.006
CAD	-0.25	-0.39 to -0.11	<0.001

Statistically significant ($p<0.05$) SDNN: Standard Deviation of NN intervals; CI: Confidence Interval; BMI: Body Mass Index; BP: Blood Pressure; HbA1c: Glycated Hemoglobin; FEV_1: Forced Expiratory Volume in 1 second; LDL: Low-Density Lipoprotein; CRP: C-Reactive Protein; NT-proBNP: N-terminal pro-brain natriuretic peptide; CAD: Coronary Artery Disease; COPD: Chronic Obstructive Pulmonary Disease

Discussion

Disease-Specific HRV Patterns in Common Chronic Diseases

The present study revealed significant reductions in HRV parameters across all chronic disease groups compared to healthy controls, with distinct patterns observed among different pathologies. Among the four chronic conditions studied, diabetes mellitus demonstrated the most profound HRV impairment, followed by coronary artery disease, hypertension, and COPD (Tables 2-5). This finding aligns with previous research indicating that diabetic autonomic neuropathy significantly impacts cardiac autonomic function. Stuckey and Petrella (2013) reported similar findings in their study, attributing the severe HRV reduction in diabetic patients to glucose-mediated neuronal damage and microvascular complications affecting autonomic nerves.

The time-domain parameters, particularly SDNN and RMSSD, showed substantial reductions across all disease groups (Table 2). SDNN, representing overall HRV, was decreased by 45.6%, 56.5%, 47.4%, and 54.0% in hypertension, diabetes, COPD, and CAD patients, respectively, compared to healthy controls. These findings corroborate the work of Almeida-Santos et al. (2016), who reported comparable SDNN reductions in hypertensive patients and associated these changes with target organ damage. Our results extend these observations across multiple chronic conditions, highlighting autonomic dysfunction as a common pathophysiological mechanism.

Frequency-domain analysis (Table 3) revealed a characteristic pattern of reduced total power, LF power, and HF power, with increased LF/HF ratio in all chronic disease groups. This pattern suggests both sympathetic and parasympathetic impairment, with a relative sympathetic predominance. The most pronounced reduction in HF power (78.4% decrease from controls) was observed in diabetic patients, indicating severe parasympathetic dysfunction. Hillebrand et al. (2013) similarly reported a significant reduction in HF power in diabetic patients and demonstrated its association with increased cardiovascular risk. Our findings of increased LF/HF ratio, particularly in COPD patients (1.72 ± 0.48), are consistent with those reported by Roque et al. (2018), who attributed this sympathovagal imbalance to hypoxemia-induced chemoreceptor activation and systemic inflammation.

Non-linear HRV parameters (Table 4) provided additional insights into the complexity and organization of heart rate dynamics in chronic diseases. The reduction in entropy measures (approximate and sample entropy) across all disease groups, most notably in diabetes mellitus, indicates decreased complexity and adaptability of cardiac autonomic control. This finding supports the work of Bellavere et al. (2019), who demonstrated that decreased complexity of heart rate dynamics in diabetic patients precedes clinical manifestations of autonomic neuropathy. The altered fractal scaling properties, evidenced by increased DFA $\alpha1$ and decreased DFA $\alpha2$ values, further highlight the disruption of normal cardiac autonomic control mechanisms in chronic diseases. Similar alterations were reported by Vanderlei et al. (2020) in hypertensive patients and were associated with increased cardiovascular risk.

The 24-hour HRV assessment in a subset of participants (Table 5) revealed consistent patterns with short-term recordings but demonstrated additional insights into circadian autonomic variations. The reduced day/night ratio across all disease groups, with the lowest values in diabetes mellitus (1.14 ± 0.16), indicates impaired circadian modulation of autonomic function. Malik et al. (2017) similarly reported blunted circadian HRV variation in CAD patients and demonstrated its prognostic significance for adverse cardiovascular events. Our findings extend this observation to other chronic conditions, suggesting that circadian autonomic dysregulation may be a common feature in chronic diseases with potential prognostic implications.

Relationship Between HRV Parameters and Clinical Variables

Correlation analysis (Table 6) demonstrated significant associations between HRV parameters and various clinical variables, with disease duration, age, glycemic parameters, and inflammatory markers showing the strongest correlations. The inverse correlation between disease duration and SDNN ($r = -0.46$, $p < 0.01$) suggests progressive autonomic dysfunction with increasing disease chronicity. This finding is consistent with the longitudinal study by Gerritsen et al. (2016), which demonstrated progressive HRV deterioration in diabetic patients over a 10-year follow-up period. The significant correlation between HbA1c and HRV parameters in our study ($r = -0.43$ for SDNN, $p < 0.01$) further supports the impact of glycemic control on autonomic function.

The correlation between inflammatory markers (CRP) and HRV parameters ($r = -0.37$ for SDNN, $p < 0.01$) highlights the potential role of inflammation in autonomic dysfunction. Williams et al. (2019) reported similar findings in their study of COPD patients and proposed that systemic inflammation may directly affect autonomic centers or indirectly impair autonomic function through effects on baroreflex sensitivity. Our results extend this observation across multiple chronic conditions, suggesting a common inflammatory pathway contributing to autonomic dysfunction.

Multiple linear regression analysis (Table 7) identified independent predictors of HRV reduction (SDNN) in chronic diseases, with disease type, age, disease duration, glycemic parameters, and NT-proBNP emerging as the strongest predictors. The significant independent association of diabetes mellitus ($\beta = -0.32$, $p < 0.001$) with reduced SDNN confirms its profound impact on autonomic function compared to other chronic conditions. This finding is consistent with the meta-analysis by Benichou et al. (2018), which identified diabetes as the strongest predictor of reduced HRV among various pathological conditions. The independent association of NT-proBNP with reduced HRV ($\beta = -0.25$, $p < 0.001$) suggests that cardiac stress and subclinical heart failure may contribute to autonomic dysfunction in chronic diseases, particularly in CAD and hypertension.

Clinical Implications of Disease-Specific HRV Patterns

The distinct HRV patterns observed across different chronic diseases have important clinical implications. In diabetes mellitus, the severe reduction in both time and frequency domain parameters, particularly HF power, suggests early and profound cardiac autonomic neuropathy that may precede clinical symptoms. This finding emphasizes the importance of early HRV assessment in diabetic patients for risk stratification and targeted interventions. Chen et al. (2020) similarly highlighted the role of HRV analysis in early detection of diabetic autonomic neuropathy and demonstrated improved outcomes with early intervention.

In hypertensive patients, the relatively preserved HF power compared to other disease groups suggests that parasympathetic function may be initially spared, with sympathetic overactivity being the predominant early feature. This finding is consistent with the work of Thayer and Lane (2018), who proposed a model of hypertension development where sympathetic overactivity precedes parasympathetic withdrawal. Our results suggest that antihypertensive strategies targeting sympathetic overactivity might be particularly beneficial in the early stages of hypertension.

The HRV pattern in COPD patients, characterized by a markedly increased LF/HF ratio (1.72 ± 0.48), indicates significant sympathovagal imbalance that may contribute to cardiovascular risk in this population. Goulart et al. (2017) similarly reported sympathetic predominance in COPD patients and demonstrated its association with increased arrhythmia risk. Our findings suggest that autonomic modulation strategies, such as breathing exercises and physical training, might be beneficial in COPD management to reduce cardiovascular risk.

In CAD patients, the reduction in overall HRV with relatively preserved non-linear parameters compared to diabetic patients suggests a different mechanism of autonomic dysfunction, possibly related to ischemia-induced neural remodeling rather than direct neural damage. Carpeggiani et al. (2021) reported similar findings and demonstrated that preserved non-linear HRV parameters in CAD patients were associated with better prognosis despite reduced time-domain measures. Our results suggest that non-linear HRV analysis might provide additional prognostic information in CAD patients beyond traditional time and frequency domain measures.

Conclusion

This comprehensive analysis of heart rate variability patterns across common chronic diseases revealed distinct autonomic signatures that reflect disease-specific pathophysiological mechanisms. All chronic conditions demonstrated significant autonomic dysfunction compared to healthy controls, with diabetes mellitus showing the most profound impairment, followed by coronary artery disease, hypertension, and COPD. The observed patterns were characterized by reduced overall HRV, impaired parasympathetic modulation, relative sympathetic predominance, decreased heart rate complexity, altered fractal scaling properties, and blunted circadian variations. These alterations correlated significantly with disease duration, glycemic parameters, inflammatory markers, and cardiac stress indicators, with multiple regression analysis identifying disease type, age, disease duration, and glycemic control as independent predictors of autonomic dysfunction. The distinct autonomic profiles across different chronic diseases provide insights into disease-specific pathophysiological mechanisms and have important implications for risk stratification, early intervention, and targeted therapeutic approaches in the management of these highly prevalent conditions.

Recommendations

Based on the findings of this study, we recommend incorporating HRV assessment into the routine clinical evaluation of patients with chronic diseases, particularly those with diabetes mellitus where autonomic dysfunction was most profound. Short-term recordings could serve as an initial screening tool with 24-hour monitoring reserved for high-risk individuals or those with borderline results. The established correlations between HRV parameters and clinical variables suggest that strategies targeting glycemic control, inflammation reduction, and cardiovascular risk factor management could potentially improve autonomic function in these populations. Disease-specific therapeutic approaches should be considered, including early parasympathetic stimulation in diabetes, sympatholytic interventions in early hypertension, breathing exercises and physical training in COPD, and ischemia prevention strategies in CAD. Longitudinal studies are needed to evaluate whether HRV-guided therapeutic interventions can improve clinical outcomes. Additionally, we recommend developing standardized protocols and reference values for HRV assessment in the Indian population, considering the potentially unique genetic, environmental, and lifestyle factors that may influence autonomic function in this demographic group.

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