Heartbeat Chronicles: Decoding the Interplay of Echocardiography and Heart Rate Variability in Chronic Heart Failure Patients – Unraveling the Mysteries with Traditional and Advanced 24-Hour Holter ECG Parameters

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Abstract

Objective: Chronic heart failure (CHF) is a clinical syndrome that encompasses individuals who either have received a definitive diagnosis of heart failure or display a gradual escalation of symptoms as time elapses. Echocardiography, particularly evaluating left ventricular function, is crucial for diagnosis and prognosis. However, 24-hour Holter monitoring, focusing on heart rate variability (HRV), provides insights into autonomic dynamics and vulnerability. Recent HRV parameters offer nuanced information, enhancing risk stratification and guiding personalized interventions in CHF. The interplay between echocardiography and HRV enables a comprehensive approach, refining the management of CHF by considering both cardiac structure and autonomic regulation. *Methods:* This prospective study at "St. Spiridon" County Hospital involved 80 patients with left ventricular ejection fraction (LVEF) < 50%. The diagnosis was according to standard clinical echocardiography, laboratory panel, and Holter ECG monitoring. *Results:* Unexpectedly, no statistically significant relationship was found between commonly used HRV parameters and echocardiographic parameters. Further analyses showed statistically significant associations between non-traditional HRV parameters and E/A ratio, E/E', and S' lateral and septal. Additionally, modifications in HRV parameters were correlated with mitral valve deceleration time, left atrial volume index, estimated pulmonary artery systolic pressure, and cardiac output. *Conclusions:* Less commonly used Holter ECG parameters, such as acceleration capacity, deceleration capacity, and triangular index, demonstrated significant diagnostic efficacy, especially when conventional HRV parameters were normal. This highlights the importance of incorporating non-traditional HRV parameters in CHF patient risk stratification, urging further exploration through comprehensive multicenter studies for long-term prognostic implications.

Keywords

Chronic Heart Failure, Heart Rate Variability, Echocardiography

Rezumat

Obiective: Insuficiența cardiacă cronică (ICC) este un sindrom caracteristic pacienților cu un diagnostic definit de insuficiență cardiacă sau care prezintă o escaladare treptată a simptomelor. Ecocardiografia, în special evaluarea funcției ventriculare stângi, este esențială atât pentru diagnostic, cât și pentru prognostic. Cu toate acestea, monitorizarea Holter ECG/24 h, în special variabilitatea ritmului cardiac, oferă perspective asupra dinamicii și variabilității autonome. Parametrii recenți ai variabilitătii ritmului cardiac oferă informații nuanțate, îmbunătățind stratificarea riscului și ghidând intervențiile personalizate în ICC. Interacțiunea dintre ecocardiografie și variabilitatea ritmului cardiac permite o abordare amplă, îmbunătățind managementul ICC. *Metoda*: Studiul prospectiv a fost condus la Spitalul "Sf. Spiridon" și a inclus un număr de 80 de pacienți, ce prezentau o fracție de ejecție a ventriculului stâng <50%. Pacienții au fost evaluați ecocardiografic, prin parametri biologici și prin monitorizare Holter ECGT/24h. *Rezultate:* În studiul de față, nu s-a obiectivat nicio corelație semnificativă statistic între parametrii variabilității ritmului cardiac utilizați în mod standard și parametrii ecocardiografici studiați. Au fost obiectivate, în schimb, asocieri semnificative între parametrii mai puțin uzuali ai variabilității ritmului cardiac și variabile ecocardiografice precum E/A, E/E' și S' lateral și septal. Mai mult decât atât, acești parametri ai variabilității ritmului cardiac au prezentat o semnificație statistică cu volumul indexat al atriului stâng, presiunea sistolică estimată în artera pulmonară și debitul cardiac. *Concluzii:* Parametrii variabilității ritmului cardiac mai puțin utilizați, precum capacitatea de accelerare, capacitatea de decelerare și indexul triunghiular, au demostrat o eficacitate diagnostică semnificativă, în timp ce nicio corelație statistică cu parametrii bine cunoscuți nu s-a obiectivat. Astfel, evidențiem importanța integrării acestor parametri în stratificarea riscului pacienților cu ICC, fiind însă necesare explorările ulterioare prin studii multicentrice, pentru a obiectiva implicațiile prognostice pe termen lung.

Cuvinte cheie

Insuficiența Cardiacă Cronică, Variabilitatea Ritmului Cardiac, Ecocardiografie

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Introduction

Heart failure transcends a mere diagnostic label, representing a multifaceted clinical syndrome arising from underlying structural and/or functional abnormality within the heart. This syndrome manifests as elevated intracardiac pressures and/or compromised cardiac output during periods of both rest and exertion. Chronic heart failure (CHF) categorizes individuals who either present with a confirmed diagnosis of heart failure or exhibit a gradual progression of symptoms over time. This distinction underscores the heterogeneous nature of heart failure, wherein diverse etiologies and clinical presentations converge under a unified syndrome characterized by impaired cardiac function and hemodynamic derangements [1-4].

Clinically, CHF manifests as a constellation of symptoms encompassing dyspnea, fatigue, peripheral edema, and exercise intolerance. The New York Heart Association (NYHA) functional classification system stratifies the severity of heart failure based on its impact on physical activity [5,6]. Concurrently, alongside the NYHA functional classification, which gauges heart failure severity in accordance with symptomatic presentation, alternative prognostic markers such as N-terminal pro-B-type natriuretic peptides (NT-proBNP) assume a pivotal role [7].

In the context of CHF, echocardiography serves as a valuable tool for elucidating cardiac abnormalities, facilitating in-depth evaluations of disease severity, and providing guidance for therapeutic decision-making [1,8]. An integral facet of echocardiographic scrutiny in CHF entails the evaluation of left ventricular function. Parameters such as left ventricular ejection fraction (LVEF), fractional shortening, and the identification of wall motion abnormalities are systematically measured to assess myocardial contractility and detect any impairment. Reduced LVEF is a prevalent observation in CHF and frequently serves as a basis for risk stratification and therapeutic strategizing [8,9]. Tissue Doppler imaging, as a technique, enables the quantification of myocardial velocities and assessment of diastolic function, thereby offering additional insights into the ventricles' relaxation properties [9].

While imaging modalities elucidate structural changes indicative of myocardial substrate, Holter monitoring assumes a complementary role by providing insights into both myocardial vulnerability and autonomic nervous system dynamics [10-12]. Holter electrocardiography (ECG) offers a means to examine heart rate variability (HRV), which serves as a reflection of the autonomic nervous system's impact on cardiac function. The association between reduced HRV in CHF and heightened susceptibility to arrhythmias, increased ventricular remodeling, and an elevated risk of sudden cardiac death has been established [13,14]. Furthermore, HRV emerges as a valuable tool for risk stratification in CHF patients, assisting clinicians in the identification of individuals at a heightened risk of adverse outcomes [14-18].

Within the realm of CHF, recently introduced HRV parameters—namely Acceleration Capacity (AC), Deceleration Capacity (DC), and the Triangular Index (TI)—have emerged as notable contributors to our comprehension of autonomic function. These non-traditional HRV parameters provide a more nuanced insight into autonomic function, surpassing the scope of traditional metrics [13,18-20]. Their evaluation in CHF augments our capability to comprehensively appraise sympathovagal balance and cardiovascular adaptability. AC, DC, and TI exhibit promise as valuable tools for risk stratification and guiding individualized therapeutic interventions in individuals with CHF [20,21]. As research in HRV progresses, these parameters may evolve into integral components of clinical assessments in CHF, thereby refining our approach to understanding and managing this intricate condition. The integrated assessment between echocardiography and HRV facilitates a more personalized and nuanced strategy in the management of CHF, considering both cardiac structure and autonomic regulation [17,19,22].

Materials and Methods

1. Study Design, Patients, and Investigations

We conducted a prospective investigation involving 80 consecutively enrolled patients who presented with CHF, had a pre-existing diagnosis of systolic heart failure, and exhibited an LVEF of less than 50%. The study took place at "St. Spiridon" County Hospital in Iasi, Romania, spanning the period from May 2023 to January 2024. Throughout the participants' hospitalization in the Cardiology Department, we vigilantly monitored their conditions.

To ensure adherence to predetermined eligibility criteria and prevent instances of acute heart failure or acute decompensation of chronic heart failure, participants were required to demonstrate clinical stability for a minimum of one month before the collection of biomarker samples and the initiation of Holter ECG/24-h monitoring. Of significance was that the participants were mandated to display an absence of indications corresponding to the principal clinical presentations, specifically, acute decompensated heart failure, acute pulmonary edema, isolated right ventricular failure, and cardiogenic shock. Additionally, the absence of a rapid or gradual onset of symptoms and signs indicative of heart failure of sufficient severity to necessitate the initiation or escalation of treatment, including intravenous therapies, were mandatory. This careful selection process aimed to ensure the inclusion of patients with stable CHF and avoid confounding factors that could impact the study's objectives.

In accordance with European Society of Cardiology (ESC) guidelines, the diagnosis of CHF necessitated the manifestation of clinical symptoms such as dyspnea, fatigue, and ankle edema. Substantiation of this diagnosis included observable signs of CHF and the objective confirmation of cardiac dysfunction through the measurement of NT-proBNP levels equal to or exceeding 125 pg/mL, supported by echocardiographic assessment [1].

Pregnant women and individuals under the age of 18 were excluded. Patients declining informed consent upon admission and those unable to undergo a thorough physical and/or echocardiographic examination due to factors like recent thoracic surgery or heightened sensory perception were part of the exclusion criteria. Additional exclusion criteria involved patients with active malignancies or receiving antineoplastic medication, individuals with

comorbid conditions associated with a life expectancy of less than one year, and those taking potentially arrhythmogenic medications. Further criteria for exclusion included patients with concurrent acute or chronic inflammatory processes, thyroid disorders, recent major surgical procedures, untreated neuropsychiatric disorders, or NT-proBNP values upon admission falling below the recommended cutoff of 125 pg/mL by the ESC. Specific patient groups with attributes that could potentially confound the interpretation of study outcomes were also excluded, such as individuals with a recent history of acute coronary syndrome within 21 days of admission, documented sustained ventricular tachycardia, atrial fibrillation, and cardiac pacemakers.

To ensure scientific rigor and reproducibility in our statistical analysis, we chose to utilize data collected exclusively at the time of patient enrollment, considering the potential variability in biomarker concentrations and clinical parameters such as blood pressure, weight, height, and body mass index over time. After obtaining informed consent, patients underwent an extensive clinical assessment, standard laboratory investigations, and a series of noninvasive diagnostic procedures, such as ECG, 24-hour Holter monitoring, and a transthoracic echocardiographic examination.

The patients' medical histories were acquired by conducting detailed anamneses and retrieving information from patients' personal files or the hospital's archives. Specific sociodemographic aspects (including age, gender, and place of residence) and particular behavioral conditions were thoroughly assessed. Additionally, underlying diseases or current medications were comprehensively evaluated. To maintain scientific integrity, comorbidities were confirmed based on either pre-existing records in the patients' personal files or diagnoses made during their hospitalization, adhering to established diagnostic criteria.

To systematically assess potential underlying causes, we conducted an extensive battery of standardized laboratory tests covering diverse parameters, including NT-proBNP, D-dimers, complete blood count, renal and hepatic function, C-reactive protein, sodium, potassium, magnesium, uric acid, total protein test, thyroid function markers, serum iron, ferritin, and glycemia. The primary objective of these tests was to rule out conditions such as infection, electrolyte imbalances, hepatic dysfunction, hypoalbuminemia, anemia, or thyroid disorders. NT-proBNP levels were quantified using the PATHFAST Cardiac Biomarker Analyzer (LSI Medience Corporation, Tokyo, Japan), employing a chemiluminescent enzyme immunoassay and the MAGTRATION® method. The manufacturer's designated reference range for NT-proBNP fell within <15–128 pg/mL.

For a comprehensive evaluation, each patient underwent a detailed echocardiography assessment utilizing the GE VividTM V7 ultrasound system (General Electric, Boston, CA, USA). The determination of LVEF followed the standardized protocol, employing Simpson's method within the two-dimensional echocardiographic apical four-chamber view. The echocardiographic assessments were conducted by two cardiologists under the supervision of a senior physician observer.

Furthermore, patients underwent 24-hour Holter ECG monitoring utilizing a twelve-channel CardioScan DMS 300–3L, a digital recorder with ten wires manufactured by DM System Company Ltd., Beijing, China. Subsequently, all recorded data underwent meticulous manual scrutiny by a cardiologist under the oversight of a senior medical practitioner, with a particular focus on assessing HRV, AC, and DC. The analysis was facilitated by the CardioScan Holter Analysis Software, specifically CardioScan 12, developed by DM Software Inc., headquartered in Beijing, China.

In accordance with our dedication to scientific rigor, periods marked by noise, artifacts, premature beats, and post-extrasystolic pauses underwent meticulous screening and were subsequently excluded from further investigation. Furthermore, individuals characterized by a high incidence of atrial and ventricular ectopic beats, specifically exceeding a frequency of more than 10 beats per hour, were deliberately excluded from the study's participant pool. This analysis rigorously excluded ectopic beats or those originating from sources outside the sinus rhythm.

Both time and frequency domain analyses of HRV, along with the assessment of AC and DC, were automatically computed and documented [23]. The time-domain indices included parameters such as the standard deviation of RR intervals for the entire duration (SDNN; normal values below 50 ms), the standard deviation of the averages of NN intervals in each 5 min segment across the entire recording (SDANN; normal values below 40 ms), the mean of the 5 min normal-to-normal intervals throughout the complete recording (SDANN index; normal values below 30 ms), the square root of the mean of the squares of the successive differences between adjacent NN intervals (RMSSD; normal values below 15), the ratio of NN50 to the total count of NN intervals (PNN50; normal values below 0.75%), and the total count of all NN intervals divided by the height of the histogram of all NN intervals, measured on a discrete scale with bins of 7.8125 ms (triangular index) [24].

The frequency-domain indices included specific frequency bands: high frequency (hF), spanning the range of 0.15 to 0.4 Hz; low frequency (lF), covering the range from 0.04 to 0.15 Hz; and very low frequency (vlF), extending from 0.0033 to 0.04 Hz [24].

The determination of DC and AC was based on an innovative phase-rectified signal averaging methodology designed for the examination of quasi-periodic oscillations within noisy and non-stationary signal data. The relative counts of deceleration and acceleration sequences, each comprising 1 to 10 RR intervals, were categorized into three risk-stratified groups: low-risk (values falling between 4.5 ms and 10 ms), intermediate-risk (ranging from 2.5 ms to 4.49 ms), and high-risk (ranging from 0 to 2.49 ms), as previously described in the literature [23].

2. Statistical Analysis

Commencing with the assessment of data distribution via the Shapiro–Wilk test, the statistical analysis was conducted using R programming language version 4.3.2. Descriptive statistics for normally distributed continuous variables included mean ± standard deviation (SD), while non-normally distributed continuous variables were summarized with the median and interquartile range (IQR:

25–75%). Categorical variables were represented by frequencies and percentages. To evaluate differences between groups, the independent samples t-test was employed for normally distributed variables, and the Mann–Whitney U test was used for variables deviating from normal distribution. Pearson's correlation coefficient (Pearson's r) was applied for parametrically distributed data to explore the correlation between parameters, whereas Spearman's rank correlation coefficient (Spearman's ρ) was used for non-parametric data to elucidate variable relationships. Categorical group comparisons were carried out using the chi-squared test. The threshold for statistical significance was established at a p-value of less than 0.05 ($p < 0.05$).

3. Ethics

The comprehensive investigation received official approval from the Ethics Committees affiliated with the Grigore T. Popa University of Medicine and Pharmacy (Approval No. 185/12.05.2022) and the Emergency Clinical Hospital St. Spiridon (Approval No. 47/14.04.2022). The entirety of the research endeavors adhered meticulously to the ethical tenets elucidated in the Declaration of Helsinki Principles, as revised in 2013. Each participating patient dutifully affixed their signature to a standardized written informed consent document, thereby manifesting their unequivocal willingness to partake in this study.

Results

1. Baseline Characteristics

The present study involved an 80-patient cohort, all diagnosed with CHF and with an LVEF below 50%. 26.3% of participants were female. The mean age of the study population was 66 ± 11 years, demonstrating diverse concurrent medical conditions. Relevant demographic and clinical characteristics are detailed in Table 1. Notably, 31.3% of patients (n = 25) had diabetes, 22.5% (n = 18) exhibited chronic kidney disease (CKD), and 25.7% (n = 22) were categorized as obese. Additionally, 48.8% (n = 39) were smokers, and 55% (n = 44) originated from rural environments. It is crucial to emphasize that, as previously explained, comprehensive blood tests revealed the absence of anemia, infection, electrolyte imbalances, and indicated normal liver and thyroid functions among the patients. Furthermore, none of the patients were prescribed medications known to induce arrhythmogenic effects.

In our study cohort, a considerable segment of patients, accounting for 46.3% or 37 individuals, presented with dyspnea classified as NYHA class II, while an additional 42.5% (34 patients) fell into NYHA class III. A minority, constituting 7.5% (6 patients), exhibited NYHA class I, and a mere 3.8% (3 patients) were categorized under NYHA class IV. The median level of NT-proBNP in our study cohort was measured at 2798 pg/mL, with values demonstrating an interquartile range from 697 to 7354 pg/mL.

Regarding therapeutic management, all enrolled patients received treatment consistent with guideline-recommended therapies, including beta-blockers, inhibitors of the renin–angiotensin–aldosterone system, mineralocorticoid receptor antagonists, and an inhibitor of sodium/glucose cotransporter 2. Notable adjustments in medication were implemented for individuals (n = 4) with CKD stages IV and V. This approach ensured adherence to established therapeutic guidelines for chronic heart failure management and addressed specific considerations for patients with advanced stages of chronic kidney disease.

Table 1 - Patient characteristics

Characteristics	All sample (n=80)
Sex	M – 59 (73.8%) F – 21 (26.3%)
Environment	R – 44 (55.0%) U – 36 (45.0%)
Smoker	YES – 39 (48.8%) NO – 41 (51.2%)
Alcohol consumption	YES – 18 (22.5%) NO – 62 (77.5%)
Diabetes	YES – 25 (31.3%) NO – 55 (68.8%)
CKD	YES – 18 (22.5%) NO – 62 (77.5%)
Obesity	YES – 22 (27.5%) NO – 58 (72.5%)
NYHA class	I – 6 (7.5%) II – 37 (46.3%) III – 34 (42.5%) IV – 3 (3.8%)

M – male; F – female; R – rural; U – urban; CKD – chronic kidney disease; NYHA- New York Heart Association

2. Heart Rate Variability and Echocardiographic parameters

Our investigation progressed to conduct comparative evaluations between echocardiographic parameters and those obtained from a 24-hour Holter ECG monitoring phase. Table 2 delineates a comprehensive summary of the analyzed parameter values. Specifically, we scrutinized HRV measures, including SDNN, SDANN, DSNN index, RMSSD, PNN50, Triangular Index (TI), vlF, lF, and hF, along with AC and DC. Within the scope of our academic investigation, it is imperative to highlight the results derived from our analysis utilizing HRV parameters and echocardiographic findings (Table 3). The normality of data distribution was evaluated using the Shapiro-Wilk test. Pearson's correlation coefficient was employed to assess the relationship between SDANN, LVEF, and cardiac output since these variables exhibited normal distribution and met the assumptions of this statistical test. Spearman's rank correlation coefficient (Spearman's rho) was utilized to explore the relationship between Holter ECG parameters and echocardiographic parameters for variables that were not normally distributed and did not meet the assumptions of parametric tests. Statistical significance was considered if $p \leq 0.05$.

It is important to highlight that we observed significant correlations between RMSSD, PNN50, TI, AC, and DC. Unexpectedly, there was no statistically significant relationship between the commonly used HRV parameters, namely SDNN, SDANN, and SDNN index, and echocardiographic parameters.

Table 2 - Summary of investigated parameter values

	Minimum	Maximum	Mean	Standard deviation
LVEDD (mm)	40	91	57.804	9.14
LVEF (%)	10	55	32	8.31
LVEDV (ml)	97	586	224.01	88.1
LVESV (ml)	55	513	157.1	76.8
E/A	0.15	3.27	1.32	0.75
E/E'	3.5	28	12.87	5.83
E/E' lateral	1.5	26	10.93	5.34
E/E' septal	5.07	34.3	15.01	7.48
S' lateral (cm/s)	0.03	0.13	0.06	0.02
S' septal (cm/s)	0.03	0.11	0.06	0.02
MV Dec T (ms)	64	685	197.92	88.16
LAVI (mL/m²)	18.52	72.08	31.63	5.83
ePASP	9	93	32.91	16.69
Cardiac output (L)	1.72	7.77	4.76	1.44
Aortic Vmax (m/sec)	0.8	4.9	1.8	1
Mean AVG (mmHg)	2.58	95	17.71	1
SDNN (ms)	32	165	81.48	29.87
SDANN (ms)	24	140	68.87	27.15
SDNN Index (ms)	17	102	40.59	18.23
RMSSD (ms)	7	93	30.45	18.48
PNN50 (%)	0	43	7.58	10.17
Triangular Index (ms)	5.5	54.2	19.8	8.7
VLF (Hz)	126.8	10314.3	1665.67	1835.99
LF (Hz)	23.8	1775.9	338.88	380.22
HF (Hz)	4.5	2202.4	195	275.96
Deceleration capacity (ms)	-4.96	9.05	3,92	2.33
Acceleration Capacity (ms)	-10.72	-1.23	-4.9	2.20

LVEDD – left ventricular end-diastolic diameter, LVEF – left ventricular ejection fraction, LVEDV – left ventricular end-diastolic voume, LVESV – left ventricular end-systolic volume, E/A – peak velocity blood flow from left ventricular relaxation in early diastole/ peak velocity flow in late diastole caused by atrial contraction, E/e' – left ventricular transmitral early diastolic filling velocity/left ventricular early diastolic myocardial velocity, E/E' lateral – peak velocity blood flow from left ventricular relaxation in early diastole/ lateral left ventricular early diastolic myocardial velocity, E/E' septal – left ventricular transmitral early diastolic filling velocity/septal wall of left ventricular early diastolic myocardial velocity, MV Dec T – mitral valve deceleration time, S' lateral – systolic excursion velocity of lateral wall of the left ventricle, S' septal – systolic excursion velocity of the septum of left ventricle, LAVI – left atrial volume index, MAPSE – mitral annular plane systolic excursion, SDNN – standard deviation of RR intervals for the entire duration, SDANN – standard deviation of the averages of NN intervals in each 5 min segment across the entire recording, SDNN index – mean of the 5 min normal-to-normal intervals throughout the complete recording, RMSSD – square root of the mean of the squares of the successive differences between adjacent NN intervals, PNN50 – the ratio of NN50 to the total count of NN intervals, hF – high frequency, lF – low frequency, vlF – very low frequency.

It is crucial to emphasize the inverse correlation of LVEF with RMSSD and PNN50, which will be discussed later. However, concerning other conventional echocardiographic parameters such as Left Ventricular End-Diastolic Diameter (LVEDD), Left Ventricular End-Diastolic Volume (LVEDV), Left Ventricular End-Systolic Volume (LVESV), aortic Vmax, and mean aortic valve gradient (AVG), no statistically significant disparities were observed with Holter ECG parameters.

In terms of the association between the E/A ratio and HRV parameters, our analysis revealed statistical significance with the TI, AC, and DC. Notably, the same HRV parameters demonstrated statistical significance with E/E' septal (TI (Spearman's ρ = −0.243, p = 0.030), AC (Spearman's ρ = 0.236, p = 0.035), DC (Spearman's ρ = −0.358, p = 0.001), and additionally PNN50 (Spearman's ρ = 0.226, p = 0.044)), while with E/E' lateral, only the correlation with TI was statistically significant (Spearman's ρ = −0.250, p = 0.024).

Although only PNN50 and the TI were statistically significant in correlation with S' lateral (PNN50 (Spearman's ρ = −0.224, p = 0.046), TI (Spearman's ρ = 0.282, p = 0.011)), multiple HRV parameters were found to be statistically significant with S' septal (RMSSD (Spearman's ρ = −0.263, p = 018), PNN50 (Spearman's ρ = −0.258, p = 0.021), TI (Spearman's ρ = 0.263, p = 0.019), AC (Spearman's ρ = −0.285, p = 0.010), DC (Spearman's ρ = 0.311, p = 0.005)).

In the context of mitral valve deceleration time (MV Dec T), notable modifications in HRV parameters were observed, demonstrating a statistically significant positive correlation with TI, AC, and DC. In relation to frequency domain parameters, a correlation was identified with very low-frequency power (Spearman's ρ = 0.290, p = 0.009) and lF (Spearman's ρ = 0.221, p = 0.049).

Surprisingly, we discovered a positive correlation between estimated pulmonary artery systolic pressure and HRV parameters, such as RMSSD (Spearman's ρ = 0.292, p = 0.009), PNN50 (Spearman's ρ = 0.278, p = 0.013), DC (Spearman's ρ = −0.316, p = 0.004), and hF (Spearman's ρ = 0.254, p = 0.023).

Lastly, cardiac output, a crucial echocardiographic parameter, exhibited statistical significance with RMSSD (Spearman's ρ = −0.237, p = 0.035), PNN50 (Spearman's ρ = −0.233, p = 0.038), and hF (Spearman's ρ = −0.280, p = 0.014).

Hence, the question arises as to whether a reduced TI or alterations in AC and DC, in contrast to other well-established HRV parameters, are associated with an increased risk of cardiovascular mortality and might represent the most modifiable parameter for HRV. This consideration is relevant, given that these parameters are comparatively less scrutinized than conventional HRV parameters. In the context of AC and DC within our study cohort, a more statistically significant correlation between echocardiographic parameters and DC was observed, an important aspect that will be further discussed.

3. Examination of Statistically Significant Parameters

The results of our study unveiled a significant association between RMSSD and PNN50 with LVEF, as depicted in Table 2. Subsequently, our inquiry sought to conduct a targeted analysis to elucidate the precise interrelationships among these parameters, as delineated in Figure 1. It is crucial to emphasize the notable weak negative correlation of LVEF with RMSSD (Spearman's ρ = −0.294, p = 0.008) and PNN50 (Spearman's ρ = −0.305, p = 0.006).

As previously indicated, our investigation revealed substantial associations between the E/A ratio and various parameters of HRV. Specifically, those exhibiting statistical significance have been

Table 3 - The relationship between Echocardiographic Parameters and Holter ECG Parameters

		SDNN	SDANN	SDNN Index	RMSSD	PNN50	Triangular Index	VLF	LF	HF	Deceleration capacity	Acceleration Capacity
LVEDD (mm)	Spearman's rho	0.096	0.064	0.105	0.215	0.201	0.003	-0.01	-0.01	0.221	-0.087	-0.124
	p-value	0.399	0.574	0.355	0.056	0.074	0.978	0.956	0.942	0.049	0.445	0.274
LVEF (%)	Spearman's rho	0.075	0.030	0.029	-0.294	-0.305	0.195	-0.01	0.039	-0.22	0.201	-0.142
	p-value	0.507	0.793	0.802	0.008	0.006	0.083	0.967	0.731	0.054	0.075	0.210
LVEDV (ml)	Spearman's rho	0.080	0.053	0.115	0.153	0.169	0.003	0.134	0.009	0.083	-0.089	-0.016
	p-value	0.479	0.638	0.311	0.175	0.134	0.977	0.237	0.935	0.467	0.433	0.886
LVESV (ml)	Spearman's rho	0.028	0.028	0.045	0.209	0.220	-0.097	0.070	-0.04	0.111	-0.191	0.074
	p-value	0.807	0.805	0.691	0.063	0.050	0.390	0.539	0.750	0.325	0.090	0.513
E/A	Spearman's rho	-0.19	-0.116	-0.218	0.127	0.139	-0.233	-0.21	-0.15	0.109	-0.381	0.226
	p-value	0.098	0.303	0.052	0.261	0.220	0.037	0.061	0.173	0.337	< .001	0.044
E/E'	Spearman's rho	-0.11	-0.051	-0.145	0.177	0.225	-0.241	-0.13	-0.18	0.146	-0.239	0.208
	p-value	0.319	0.653	0.199	0.116	0.045	0.031	0.239	0.121	0.196	0.033	0.064
E/E' lateral	Spearman's rho	-0.13	-0.065	-0.140	0.123	0.218	-0.250	-0.13	-0.16	0.129	-0.115	0.091
	p-value	0.240	0.565	0.216	0.278	0.053	0.024	0.247	0.152	0.254	0.311	0.424
E/E' septal	Spearman's rho	-0.15	-0.099	-0.142	0.211	0.226	-0.243	-0.17	-0.18	0.142	-0.358	0.236
	p-value	0.187	0.383	0.210	0.060	0.044	0.030	0.135	0.111	0.208	0.001	0.035
S' lateral (cm/s)	Spearman's rho	0.122	0.074	0.092	-0.206	-0.224	0.282	-0.01	0.048	-0.20	0.163	-0.150
	p-value	0.281	0.513	0.418	0.066	0.046	0.011	0.959	0.674	0.078	0.149	0.183
S' septal (cm/s)	Spearman's rho	0.116	0.107	0.102	-0.263	-0.258	0.263	0.064	0.096	-0.22	0.311	-0.285
	p-value	0.306	0.347	0.366	0.018	0.021	0.019	0.571	0.399	0.051	0.005	0.010
MV Dec T (ms)	Spearman's rho	0.221	0.125	0.222	-0.022	-0.010	0.251	0.290	0.221	0.027	0.309	-0.293
	p-value	0.049	0.270	0.048	0.847	0.931	0.025	0.009	0.049	0.813	0.005	0.008
LAVI (mL/m²)	Spearman's rho	0.049	0.013	0.118	0.304	0.278	0.001	0.100	0.015	0.261	-0.208	-0.080
	p-value	0.669	0.910	0.296	0.006	0.010	0.990	0.376	0.895	0.019	0.065	0.479
ePASP	Spearman's rho	-0.01	-0.039	-0.045	0.292	0.278	-0.101	-0.17	-0.07	0.254	-0.316	0.064
	p-value	0.975	0.732	0.694	0.009	0.013	0.373	0.138	0.512	0.023	0.004	0.570
Cardiac output (L)	Spearman's rho	0.030	0.107	-0.027	-0.237	-0.233	-0.032	0.084	0.053	-0.28	0.003	0.066
	p-value	0.795	0.346	0.814	0.035	0.038	0.779	0.460	0.646	0.014	0.981	0.564
Aortic Vmax (m/sec)	Spearman's rho	0.004	-0.069	0.019	0.024	-0.011	0.009	0.072	0.103	0.008	0.151	-0.119
	p-value	0.975	0.543	0.864	0.833	0.921	0.934	0.524	0.365	0.943	0.181	0.295
Mean AVG (mmHg)	Spearman's rho	-0.05	-0.063	0.003	0.012	-0.005	-0.050	0.075	-0.12	-0.03	0.099	-0.073
	p-value	0.638	0.577	0.976	0.918	0.963	0.658	0.506	0.273	0.823	0.384	0.520

LVEDD – left ventricular end-diastolic diameter, LVEF – left ventricular ejection fraction, LVEDV – left ventricular end-diastolic voume, LVESV – left ventricular end-systolic volume, E/A – peak velocity blood flow from left ventricular relaxation in early diastole/ peak velocity flow in late diastole caused by atrial contraction, E/e' – left ventricular transmitral early diastolic filling velocity/left ventricular early diastolic myocardial velocity, E/E' lateral – peak velocity blood flow from left ventricular relaxation in early diastole/ lateral left ventricular early diastolic myocardial velocity, E/E' septal – left ventricular transmitral early diastolic filling velocity/septal wall of left ventricular early diastolic myocardial velocity, MV Dec T – mitral valve deceleration time, S' lateral – systolic excursion velocity of lateral wall of the left ventricle, S' septal – systolic excursion velocity of the septum of left ventricle, LAVI – left atrial volume index, MAPSE – mitral annular plane systolic excursion, SDNN – standard deviation of RR intervals for the entire duration, SDANN – standard deviation of the averages of NN intervals in each 5 min segment across the entire recording, SDNN index – mean of the 5 min normal-to-normal intervals throughout the complete recording, RMSSD – square root of the mean of the squares of the successive differences between adjacent NN intervals, PNN50 – the ratio of NN50 to the total count of NN intervals, hF – high frequency, lF – low frequency, vlF – very low frequency.

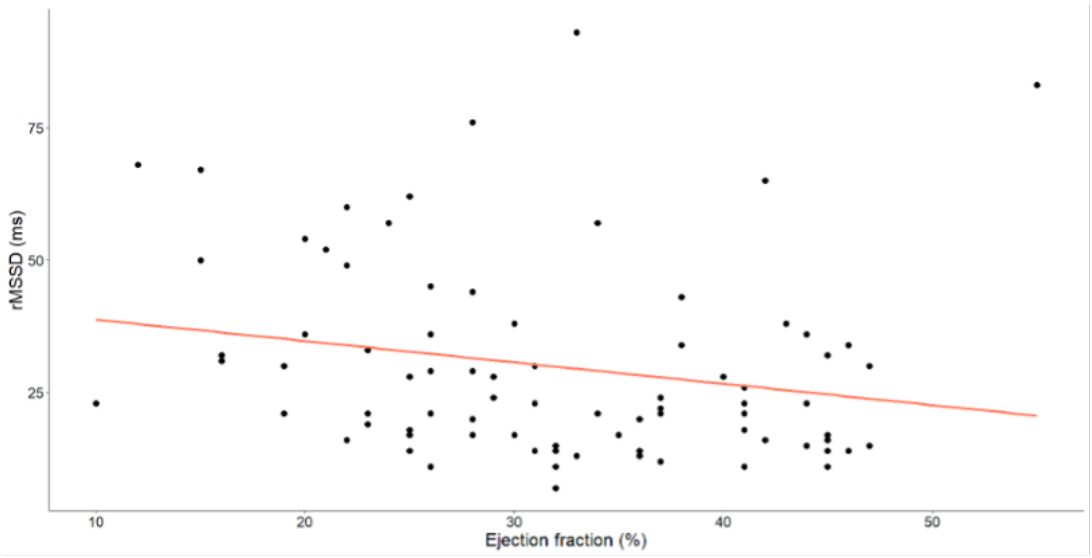


Figure 1 - Correlation between left ventricular ejection fraction (%) and RMSSD (ms). RMSSD—square root of the mean of the squares of the successive differences between adjacent NN intervals.

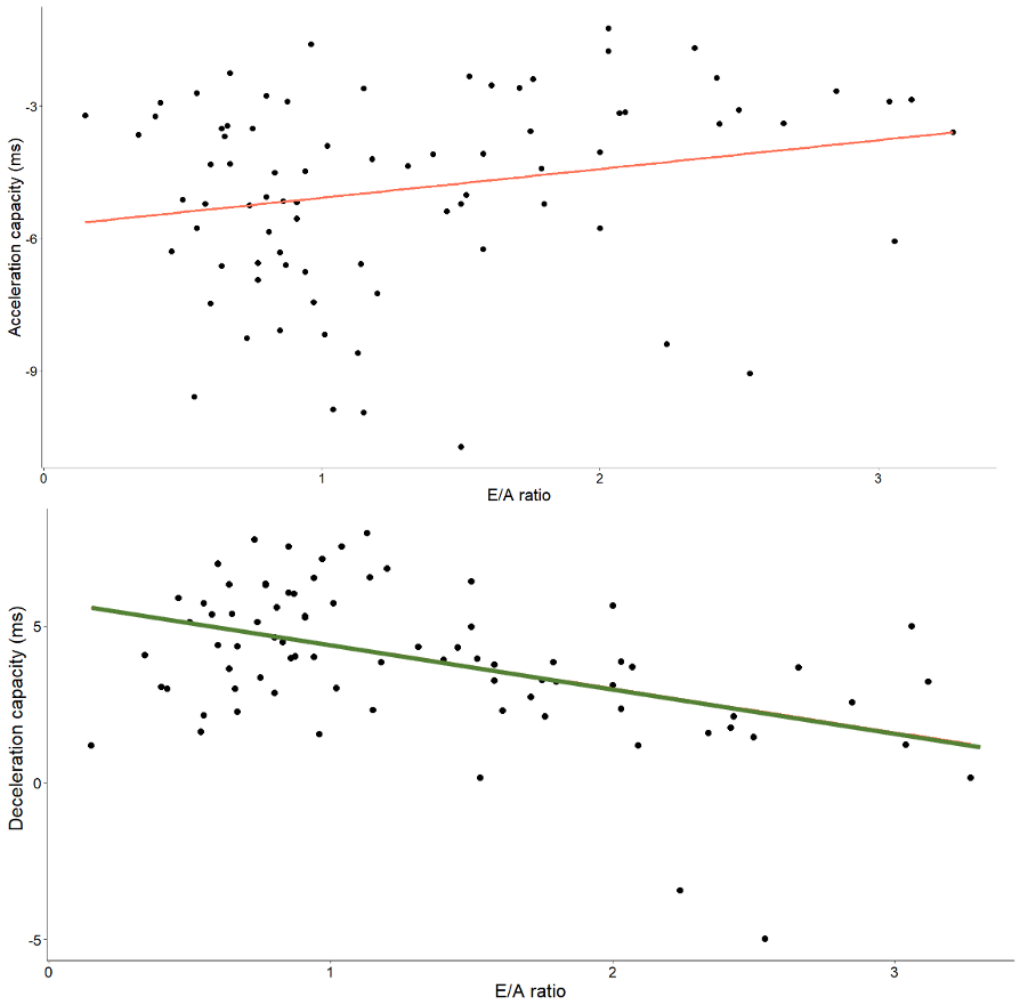


Figure 2 - Association between the E/A ratio and both acceleration (ms) and deceleration capacity (ms).

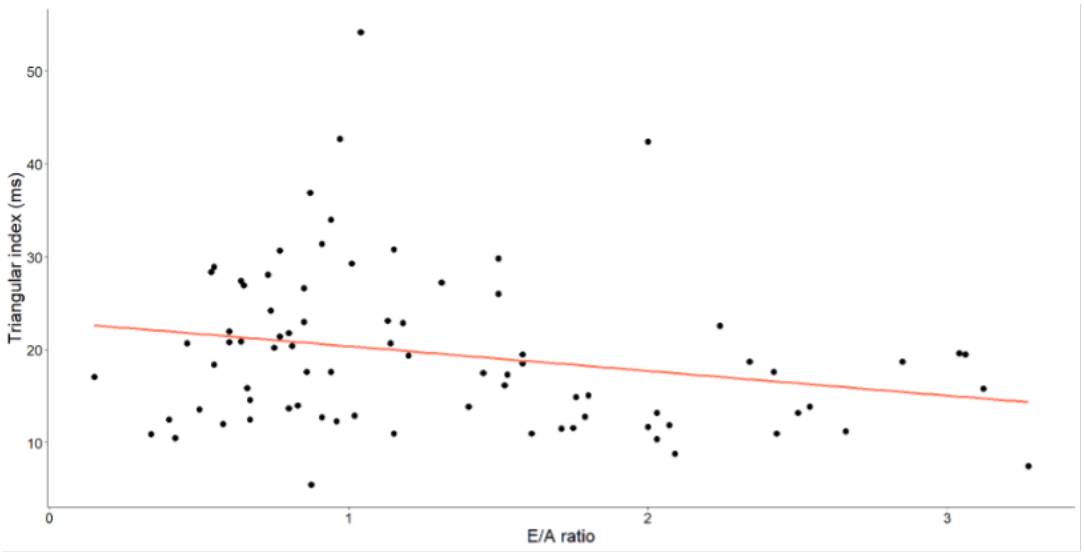


Figure 3 - Correlation between the E/A ratio and the Triangular Index (ms).

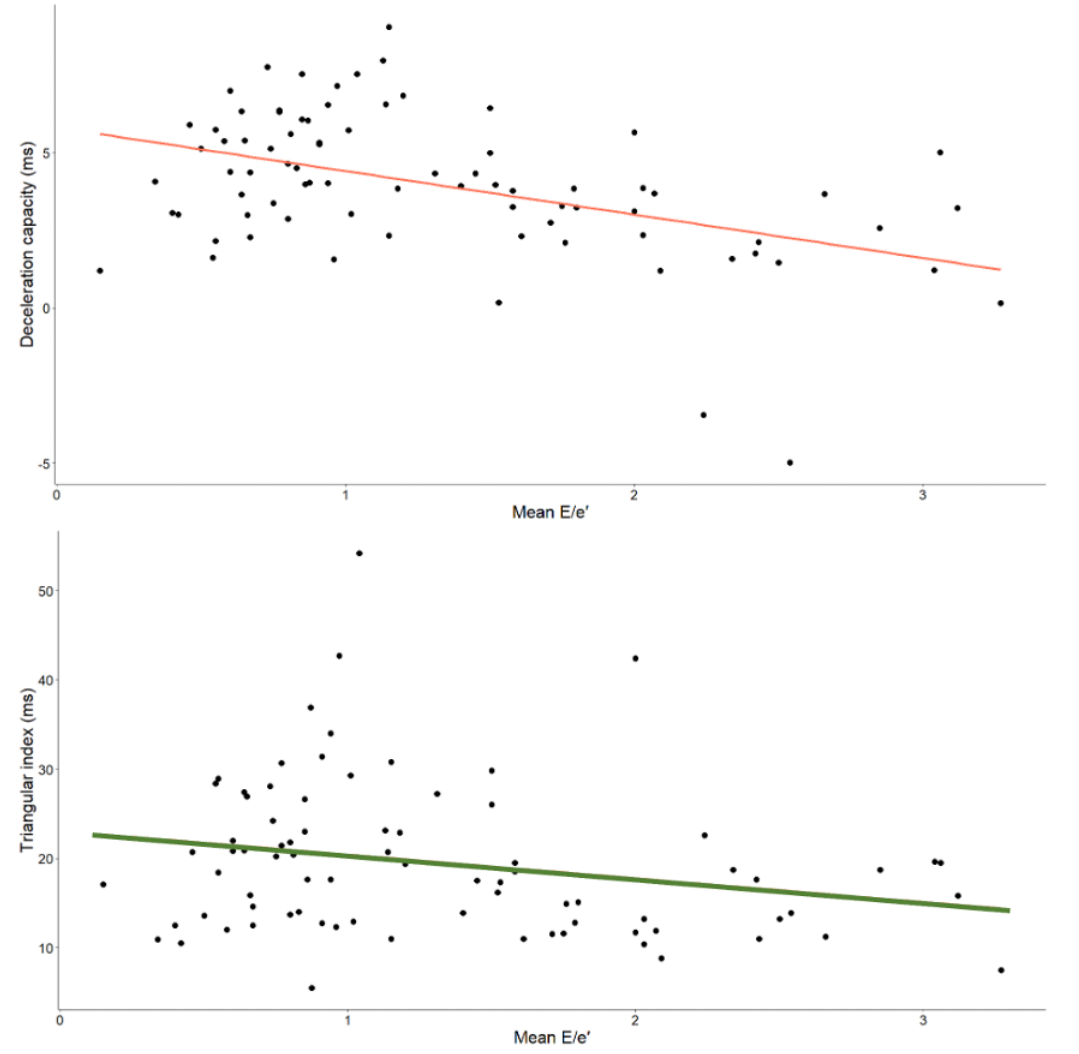


Figure 4 - Correlation between the E/E' ratio and both deceleration capacity (ms) and the Triangular Index (ms).

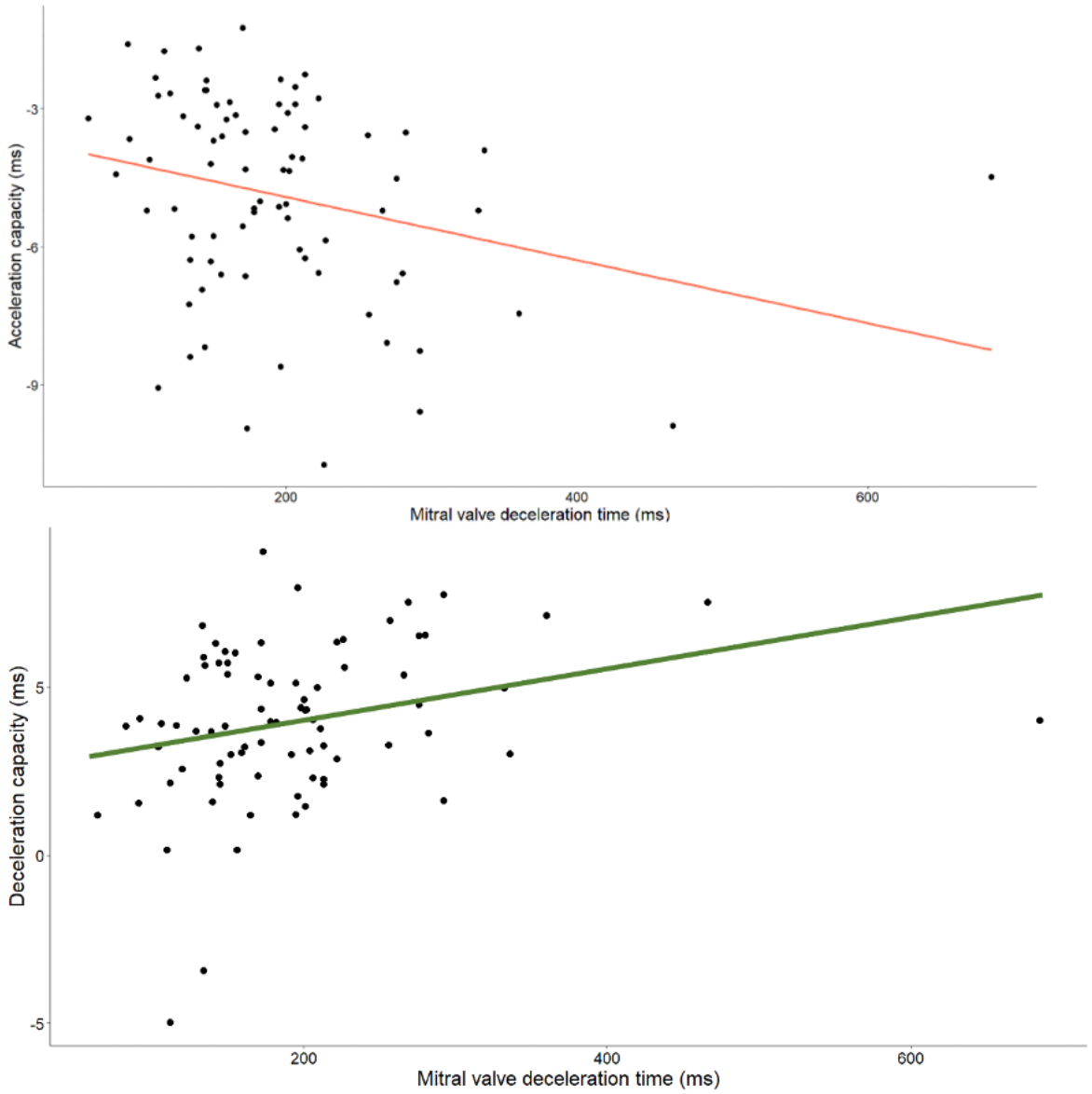


Figure 5 - Association between mitral valve deceleration time (ms) and both acceleration (ms) and deceleration capacity (ms).

comprehensively scrutinized and are delineated in Figures 2 and 3. A statistically significant, weak-to-moderate positive correlation was discerned between AC and the E/A ratio (Spearman's ρ = 0.226, p = 0.044). Furthermore, a statistically significant, weak negative correlation was observed between DC and the E/A ratio (Spearman's ρ = −0.381, p < 0.001). Lastly, a statistically significant negative association, characterized as weak-to-moderate (Spearman's ρ = −0.233, p = 0.037), was identified between the TI and the E/A ratio.

A statistically significant, weak-to-moderate positive correlation was discerned between the E/E' ratio and PNN50 (Spearman's ρ = 0.225, p = 0.045). Furthermore, a weak-to-moderate negative correlation between the E/E' ratio and both DC (Spearman's ρ = −0.230, p = 0.033) and TI (Spearman's ρ = −0.241, p = 0.031) was observed (Fig. 4).

In the evaluation of MV Dec T, our aim was to underscore the additional significance conferred by AC and DC, along with TI, as depicted in Figure 5. Therefore, notable modifications in HRV parameters were observed, demonstrating a statistically significant weak-to-moderate positive correlation with TI (Spearman's ρ = 0.251, p = 0.025), a weak negative association with AC (Spearman's ρ = −0.293, p = 0.008), and a weak positive association with DC (Spearman's ρ = 0.309, p = 0.005).

As anticipated, an additional important echocardiographic parameter, namely the left atrial volume index (LAVI), exhibited a weak positive correlation with both RMSSD (Spearman's ρ = 0.304, p = 0.006) and PNN50 (Spearman's ρ = 0.278, p = 0.010), as illustrated in Figure 6.

Discussion

Echocardiography assumes an indispensable role in the comprehensive management of CHF, given its noninvasive nature, wide accessibility, and real-time information provision. Echocardiography is crucial not only for the initial diagnosis and characterization of CHF but also for monitoring disease progression and assessing the response to therapeutic interventions. This necessitates the confluence of clinical symptoms or signs indicative of CHF alongside objective evidence of cardiac dysfunction [1].

While continuous ambulatory Holter ECG monitoring has traditionally been considered secondary in heart failure diagnosis, its evolving understanding reveals its potential as a valuable tool for investigating the intricate factors contributing to the mechanisms of sudden death. Thus, continuous ambulatory Holter ECG monitoring, often downplayed in conventional wisdom, plays a pivotal role in risk stratification [25-27].

Our investigation results indicate that specific echocardiographic parameters in CHF patients lead to an augmentation of certain less conventional Holter ECG parameters related to HRV, even as other parameters maintain values within the normal range. Within the context of our study, statistically significant deviations from normal values are observed for both the TI and the acceleration and deceleration capacity concerning certain echocardiographic parameters.

As previously delineated, among the echocardiographic parameters investigated, we observed a more pronounced and statistically significant correlation with DC compared to AC. The rationale underlying the potential predilection for DC to be affected before AC in certain circumstances may be attributed to the dynamic characteristics inherent in the autonomic nervous system response, influenced by various factors [28-31].

Nevertheless, as our results have shown, a weak correlation among those HRV parameters may stem from multifaceted determinants inherent within physiological, pathological, and environmental domains. These factors encompass a broad spectrum of influences, ranging from intrinsic autonomic modulation to extrinsic perturbations, each exerting variable effects on HRV metrics. Consequently, the presence of uncontrolled or heterogeneously distributed factors across the study cohort can attenuate the strength of associations observed among HRV parameters [32]. Moreover, HRV parameters encapsulate distinct facets of autonomic nervous system dynamics and cardiac physiology. Variations in their physiological underpinnings, including differential sensitivity to parasympathetic and sympathetic modulation, contribute to the nuanced landscape of inter-parameter correlations [33]. Consequently, weak associations between HRV metrics may reflect the intricate interplay between divergent autonomic branches and broader physiological mechanisms. Methodological considerations further underscore the complexity inherent in HRV research [32,34]. Variability in data acquisition methodologies, signal processing algorithms, and parameter selection can introduce inherent variability and systematic biases, thereby influencing the observed correlations between HRV parameters. Additionally, demographic heterogeneity within study cohorts, encompassing age, gender, prevalent comorbidities, and pharmacological interventions, introduces confounding influences that impinge upon the interpretative clarity of HRV data [32-34].

Concerning one of the widely utilized echocardiographic parameters, namely LVEF, our investigation has revealed a statistically significant association with RMSSD and PNN50. Elevated RMSSD values generally correlate with heightened parasympathetic tone and improved autonomic balance. Concurrently, PNN50 serves as an indicator of parasympathetic activity, with increased values signifying heightened parasympathetic tone. The positive correlation identified between LVEF and both RMSSD and PNN50 suggests a potential link wherein individuals exhibiting superior cardiac function (indicated by higher LVEF values) also demonstrate heightened parasympathetic activity (indicated by higher RMSSD and PNN50 values) [30,32,35]. However, while LVEF and both RMSSD and PNN50 parameters offer insights into cardiac performance, their disparate physiological underpinnings suggest that they may not consistently exhibit strong associations, as LVEF serves as an indicator of left ventricular contractile function, while Holter ECG parameters primarily reflect autonomic nervous system activity and its impact on short-term HRV. A weak association can be ascribed to the presence of confounding variables, such as age, medication usage, comorbidities, and physiological states, which could contribute to the attenuated correlation observed between RMSSD and LVEF. Pharmacological interventions affecting heart rate variability or myocardial contractility, for instance, may introduce variability in the relationship between these parameters [32,33,35]. In alignment with our findings, Alkhodari et al. reported a positive correlation between HRV parameters and LVEF, underscoring the significance of circadian 24-hour cycle analysis [36]. This suggests that compromised cardiac function might coincide with alterations in autonomic nervous system equilibrium [32-34]. Corroborating our study, Birand et al. observed a positive and significant correlation between the parasympathetic band of HRV and LVEF, reinforcing our findings ($p < 0.0001$) [37].

Concerning diastolic function, our investigation has revealed a positive correlation between the E/A ratio and TI, AC, and DC. Additionally, a positive correlation has been identified between the E/E' ratio and TI. This indicates a potential connection between variations in diastolic function and the dynamics of blood flow during diastole, providing valuable insights into the hemodynamics, mechanics, and autonomic nervous system of the heart during the relaxation phase [38,39]. However, while both metrics relate to cardiac function, they represent distinct physiological aspects, and their correlations may be influenced by differential regulatory mechanisms. E/A ratio and HRV parameters may exhibit dynamic fluctuations over time, influenced by acute physiological changes or short-term interventions. As such, cross-sectional assessments may not fully capture the transient nature of these metrics, potentially leading to weaker associations in certain contexts [39,40].

The correlation between HRV and E/e' (whether measured at the septal or lateral site) may be influenced by diverse physiological

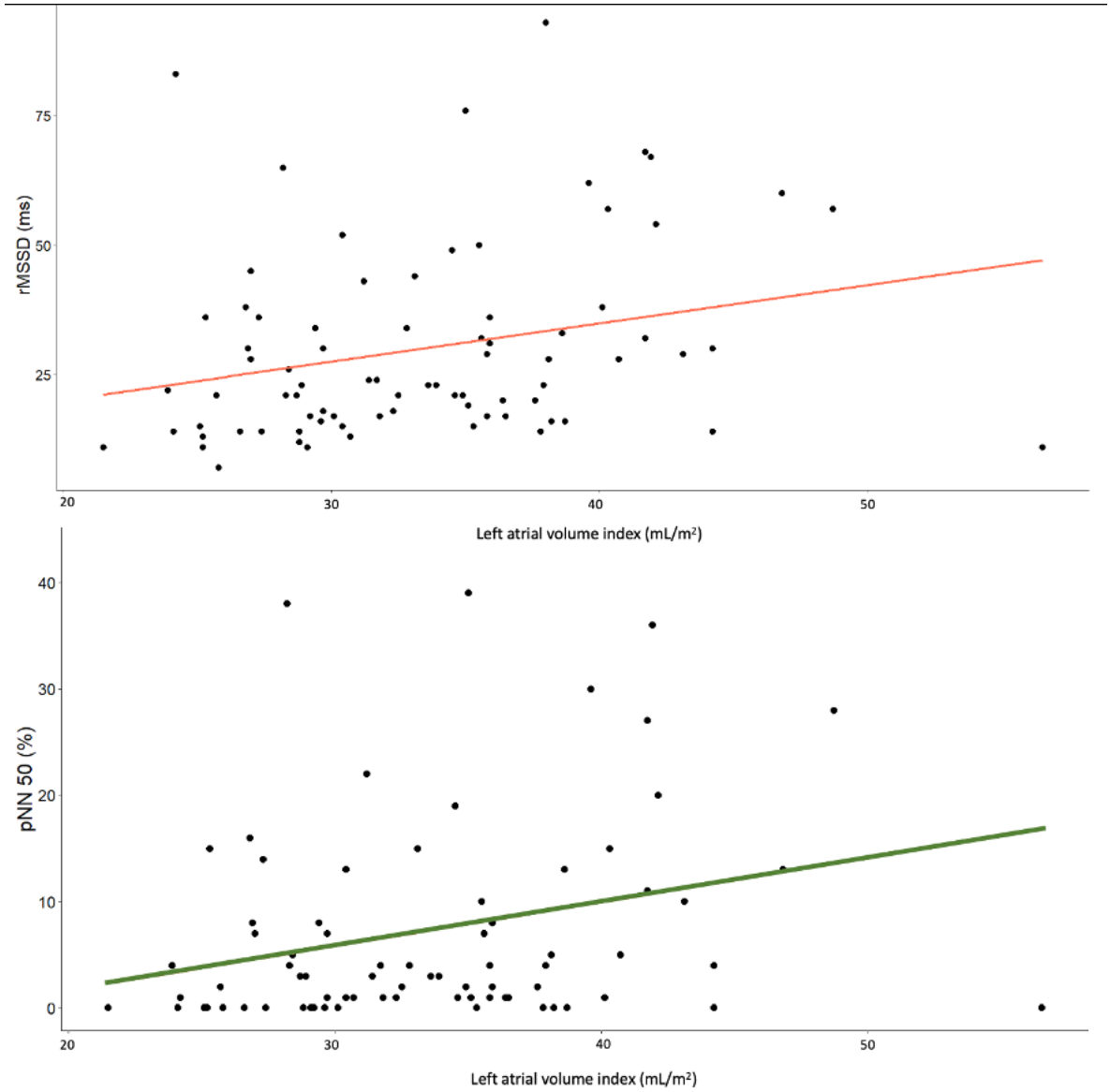


Figure 6 - Association between the left atrial volume index (mL/m²) and RMSSD (ms) as well as PNN50 (%). RMSSD—square root of the mean of the squares of the successive differences between adjacent NN intervals, PNN50—ratio of NN50 to the total count of NN intervals.

and clinical factors. The septal region, with its closer anatomical and functional relationship with the cardiac conduction system and autonomic nerve fibers, may be more directly linked to autonomic modulation, leading to a more robust correlation with HRV [38-40]. Conversely, the lateral annulus, influenced by the left ventricular free wall, may possess distinct mechanical and sympathetic innervation characteristics, impacting the relationship between E/e' lateral and HRV. However, the weak correlation in our study between HRV and E/e' (at either septal or lateral sites) can be influenced by specific clinical conditions of the patients under study. Pathological changes such as myocardial ischemia or fibrosis may impact the correlation differently at the septal and lateral annuli. Another echocardiographic parameter related to diastolic function that demonstrated a statistically significant correlation with TI, AC, and DC is MV Dec T [38-41].

The final significant echocardiographic parameter demonstrating a correlation with HRV parameters is the LAVI. Heightened parasympathetic activity, as indicated by elevated RMSSD and PNN50, may engender increased HRV, potentially influencing left atrial filling and size [41,42]. However, it is imperative to note that vagal tone, represented by higher RMSSD, directly affects the heart, including the atria. Elevated parasympathetic activity fosters atrial relaxation and impacts atrial compliance. Shifts in atrial function, orchestrated by autonomic modulation, may consequently contribute to alterations in left atrial volume over time [8,9,42].

The established correlation bears clinical significance, as changes in left atrial volume can serve as indicative markers for various cardiovascular conditions, encompassing atrial fibrillation, heart failure, or other structural heart abnormalities. Parsi et al. employed ECGs in their study to predict the presence of paroxysmal

atrial fibrillation [43]. Analogously, comparable scoring systems utilizing HRV parameters derived from Holter ECG investigations could be applied on a broader scale, particularly in patients exhibiting no paroxysmal atrial fibrillation on standard ECG assessments [42,43].

Crucially, these alterations of AC, DC, and TI were not discernible in other frequently employed parameters assessing HRV. However, various comorbidities, such as diabetes, CKD, or obesity, possess the capacity to exert influence on the dysregulation of the autonomic nervous system, consequently impacting the parameters of HRV [44]. The disruption of the autonomic nervous system, in turn, perturbs the electrical stability of the heart, potentially leading to alterations in HRV. Perturbations in blood glucose levels, disruptions in electrolyte balance, chronic inflammatory processes, oxidative stress, insulin resistance, and the presence of metabolic syndrome further contribute to disturbances in cardiac rhythm. It is noteworthy that diabetes can engender structural and functional changes in cardiac tissue, a condition commonly referred to as diabetic cardiomyopathy [44,45]. CKD, characterized by the accumulation of uremic toxins within the body, engenders a myriad of repercussions for the cardiovascular system. These toxins have the capacity to stimulate myocardial fibrosis, incite inflammatory responses, and induce oxidative stress, collectively influencing the electrical properties of the heart [44,46]. These alterations collectively foster an environment conducive to the development of arrhythmogenic tendencies within the cardiac milieu [44-46]. Given the statistically significant nature of these identified parameters, which have not undergone exhaustive exploration, we advocate for subsequent investigations to systematically examine these parameters, also in relation to different comorbidities and echocardiographic parameters. This recommendation is rooted in the potential of these parameters to function as early indicators of autonomic nervous system dysregulation, facilitating timely identification and intervention in individuals affected by such dysregulation.

As previously outlined, all participants underwent supervised therapy for heart failure, inclusive of beta-blockade, recognized as a primary determinant influencing HRV. Prospective investigations, encompassing diverse beta-blockers and their respective dosages, are imperative to ascertain not only their direct impact on HRV parameters but also to elucidate potential interactions between different beta-blockers and HRV. Such comprehensive exploration is essential for refining our understanding of the nuanced effects of beta-blockade on HRV across various patient populations and clinical contexts. Additionally, considering the wide range of beta-blockers available, including those with varying pharmacokinetic and pharmacodynamic profiles, a thorough investigation can provide valuable insights into optimizing treatment strategies for heart failure while minimizing adverse effects on HRV. Furthermore, forthcoming research endeavors should explore the potential influence of environmental factors, lifestyle choices, and habits such as smoking or alcohol consumption on HRV parameters, with a view toward extending current understanding. Concerning the etiology of HF within our cohort, all individuals presented with ischemic origins, confirmed via coronary angiography, revealing lesions exceeding 75% in at least one coronary artery. Nonetheless, it is noteworthy that some patients may concurrently manifest alcohol-induced cardiomyopathy. Hence, future studies should contemplate diverse etiological pathways to comprehensively investigate their implications on HRV.

While our study did not assess long-term adverse cardiovascular outcomes, numerous investigations have established their prognostic capacity for significant adverse cardiovascular events [28-30,34,40]. To address this limitation, we aim to integrate data on long-term cardiovascular events and extend our follow-up in future investigations.

The application of Holter ECG monitoring and echocardiography in individuals with CHF holds the potential not only to enhance risk stratification but also to inform early therapeutic interventions, thereby contributing to an improvement in overall quality of life. LVEF assumes paramount significance in the decision-making process regarding eligibility for defibrillator implantation, with LVEF values at or below a commonly accepted threshold of 35% serving as an indication for primary prevention. However, risk assessment in this context is characterized by its multifactorial nature. Guidelines extend considerations beyond LVEF, encompassing additional variables such as the NYHA functional class, NT-proBNP levels, age, comorbidities, and medication usage. Moreover, the underlying etiology of heart failure, whether ischemic or non-ischemic, plays a pivotal role in prognosis, with ischemic heart disease potentially associated with an elevated risk of adverse events [1].

In terms of future perspectives, the application of machine learning (ML) algorithms holds promise in the analysis of extensive datasets comprising echocardiographic images and HRV measurements. These algorithms possess the capability to discern subtle patterns and associations that may elude human observers, thereby advancing diagnostic capabilities and enhancing risk prediction [47,48]. There exists the potential to develop predictive models utilizing echocardiographic parameters and HRV data, enabling the assessment of an individual's cardiovascular disease risk and facilitating early intervention through personalized treatment plans. Additionally, ML algorithms may be leveraged to forecast episodes of decompensation or exacerbation in CHF [49]. Timely detection of impending heart failure decompensation could facilitate interventions, potentially reducing hospitalizations and enhancing patient outcomes [49-51].

Furthermore, ML models can analyze longitudinal changes in HRV and echocardiographic parameters, offering insights into treatment responses. This continuous monitoring approach enables clinicians to tailor interventions based on individual patient responses, thereby optimizing therapeutic strategies [47,50]. Lastly, ML technologies stand poised to support the remote monitoring of CHF patients via wearable devices capable of capturing real-time HRV data. The integration of machine learning with such wearable devices holds the potential to provide continuous and non-invasive insights into cardiovascular health [52,53].

Limitations of the Study

The principal constraint arises from the monolithic nature of the study's singular-center framework and the comparatively limited enrollment of patients. Nevertheless, it is imperative to underscore the scrupulous application of comprehensive exclusion criteria designed to scrutinize HRV parameters while mitigating the influence of concurrent comorbidities. Additional investigations are imperative to delineate forthcoming trajectories that integrate a more comprehensive population, encompassing varied comorbidities, with adherence to exclusionary parameters, thereby facilitating a nuanced understanding of their potential implications on HRV. Moreover, broadening the scope of the investigation to encompass a more expansive patient cohort would facilitate the implementation of multivariable regression analysis and the formulation of a multi-parameter risk stratification score. The statistical methodology employed encompassed HRV variables and echocardiographic parameters. Future investigations should employ more advanced statistical models, integrating potential confounding factors such as NTproBNP or other biomarkers. Furthermore, longitudinal studies focusing on the enduring impact of these HRV parameters on the studied patient cohort constitute a focal point of our forthcoming investigation. Additionally, the primary endpoint for future research endeavors will center on the longitudinal trajectory, specifically examining whether these parameters correlate with in-hospital mortality rates, incidences of hospital readmission, or the development of various atrial or ventricular arrhythmias. Significantly, the omission of patients with heart failure with preserved ejection fraction necessitates exploration in subsequent research endeavors. Finally, it is imperative to accentuate that our study cohort, predominantly comprising patients with chronic heart failure, spans diverse disease stages, introducing heterogeneity that demands consideration in forthcoming inquiries.

Conclusions

Our study aimed to broaden the clinical applicability of HRV measured through a 24-hour Holter ECG in individuals with CHF and explore its correlation with echocardiographic parameters. Holter ECG parameters, including acceleration and deceleration capacity, as well as the triangular index, represent fewer mainstream metrics within the realm of cardiac monitoring. Despite their relatively limited utilization, these metrics exhibit considerable potential as focal points for in-depth investigation in forthcoming research pursuits. The incorporation of these parameters into future studies could hold promise for elucidating novel aspects of cardiac function and autonomic regulation, thereby enriching our understanding of cardiovascular physiology and pathophysiology.

It is important to highlight that well-established HRV parameters such as SDNN, SDNN index, and SDANN did not exhibit discernible associations with echocardiographic parameters. Conversely, non-traditional parameters displayed statistically significant correlations, hinting at a potential influence of heart failure medications on conventional HRV parameters and necessitating further exploration.

These findings underscore the importance of integrating non-traditional HRV parameters into the risk stratification process for CHF patients, proposing a transformative approach to utilizing these parameters as prognostic tools across diverse patient populations. However, it is crucial to underscore the need for comprehensive multicenter studies to validate the long-term prognostic implications of these findings.

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Conflict of interest

The authors have no conflicts of interest to declare.

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List of abbreviations

AC, acceleration capacity
AVG, aortic valve gradient
CHF, chronic heart failure
CKD, chronic kidney disease
DC, deceleration capacity
E/A, peak velocity of blood flow during left ventricular relaxation in early diastole/peak velocity of flow in late diastole caused by atrial contraction
E/e′, left ventricular transmitral early diastolic filling velocity/left ventricular early diastolic myocardial velocity
ECG, electrocardiography
ESC, European Society of Cardiology
hF, high frequency
HRV, heart rate variability
LAVI, left atrial volume index
lF, low frequency
LVEDD, left ventricular end-diastolic diameter
LVEDV, left ventricular end-diastolic volume
LVEF, left ventricular ejection fraction
LVESV, left ventricular end-systolic volume
MAPSE, mitral annular plane systolic excursion

ML, machine learning
MV Dec T, mitral valve deceleration time
NT-proBNP, N-terminal pro-B-type natriuretic peptides
NYHA, New York Heart Association
PNN50, ratio of NN50 to the total count of NN intervals
RMSSD, square root of the mean of the squares of the successive differences between adjacent NN intervals
S′ lateral, systolic excursion velocity of the lateral wall of the left ventricle
S′ septal, systolic excursion velocity of the septum of the left ventricle
SDNN, standard deviation of RR intervals for the entire duration
SDANN, standard deviation of the averages of NN intervals in each 5 min segment across the entire recording
SDNN index, mean of the 5 min normal-to-normal intervals throughout the complete recording
vlF, very low frequency
TI, triangular index

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