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ORIGINAL ARTICLE

Short-term heart rate variability: A potential approach to frailty assessment in older adults

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Abstract

Objectives: This study aimed to evaluate cardiac autonomic modulation using short-term heart rate variability (HRV) and compare it among frailty statuses in older Indian adults.

Methods: A total of 210 subjects aged 60 years and above were recruited into three groups: frail ($n=70$), pre-frail ($n=70$), and non-frail ($n=70$) from the outpatient department of Geriatric Medicine at a tertiary care hospital in India. Frailty status was assessed using the Rockwood frailty index (FI) criteria. HRV was derived from a 5-min ECG recording of standard limb leads and assessed using time domain, frequency domain, and nonlinear analysis of cardiac interval variability.

Results: The HRV parameters indicative of parasympathetic modulation such as SDNN, SDSD, rMSSD, NN50, pNN50, absolute HF power, and SD1 were significantly lower in frail subjects compared with both pre-frail and non-frail subjects ($P<0.05$). Absolute LF power and SD2 were also lower in frail subjects compared with pre-frail and non-frail subjects ($P<0.05$). Measures of sympatho-vagal balance (LF/HF and SD1/SD2 ratios) did not show statistical significance. The FI demonstrated negative correlations with all HRV parameters.

Conclusions: Frail individuals exhibit decreased sympathetic and parasympathetic modulation compared with pre-frail and non-frail individuals, although maintaining a balanced sympatho-vagal state. Furthermore, autonomic modulation declines progressively with increasing frailty.

KEYWORDS
autonomic modulation, frailty, heart rate variability

1 | INTRODUCTION

The autonomic nervous system (ANS) plays a pivotal role in maintaining homeostasis, which is crucial for the proper functioning of physiological processes. In challenging environments or when faced with stressors, whether internal (such as diseases) or external (such as daily activities), the ANS coordinates with other physiological systems to preserve this balance. This coordination becomes especially critical during stress responses, where rapid adjustments are needed to adapt to changing conditions.[1,2] Age and disease-related deterioration in

homeostatic regulatory mechanisms leads to the loss of complexity in their output such as loss of intricacies in heart rate signals due to the degradation of cardiac autonomic control.[3,4] However, as individuals age or experience certain diseases, the regulatory mechanisms responsible for maintaining homeostasis can deteriorate. This deterioration often manifests as a loss of complexity in the signals generated by these regulatory mechanisms. For example, in the context of cardiac autonomic control, this loss of complexity can be observed as a simplification or reduced variability in heart rate signals.

Frailty in older adults is characterized by a decline in multiple physiological systems and a reduction in physiological reserves, leading to increased vulnerability to stressors. This syndrome represents a critical loss of physiological complexity, which impairs the individual's ability to maintain homeostasis, particularly under conditions of stress.[5–7] The ANS is fundamental in regulating various bodily functions to achieve and maintain homeostasis. It controls involuntary processes such as heart rate, blood pressure, digestion, and respiratory rate. Given its role in adaptability and plasticity, particularly in response to stressors, the ANS becomes a crucial component to assess in understanding frailty.

Cardiac control by the ANS can be assessed through the analysis of heart rate variability (HRV), which involves studying the variations in the time intervals between successive heartbeats, derived from electrocardiogram (ECG) signals.[8,9] This noninvasive method provides valuable insights into ANS function and its influence on cardiovascular regulation.[10] HRV reflects the dynamic interplay between the sympathetic and parasympathetic branches of the ANS. Specifically, high HRV typically indicates a healthy balance with predominant parasympathetic (vagal) activity, which is associated with adaptive responses to stress, resilience, and better overall health outcomes. Conversely, reduced HRV often signifies higher sympathetic activity or diminished vagal tone, which can indicate physiological stress, cardiovascular dysfunction, or increased risk of adverse health events.[11–13]

Few studies have investigated the relationship between frailty and HRV using long-duration ECG.[12,13] However, this is not practical in day-to-day practice. As measuring long-term variability by long-duration ECG can be cumbersome and nonpractical, short-term variability can be used for practical purposes. A study comparing long-term and short-term HRV analyzes in ischemic cardiomyopathy patients found a significant difference in frequency and nonlinear dynamics between the two methods.[14] However, no such comparative study has been done concerning frailty as per our knowledge. In this study, we have investigated the relationship between cardiac autonomic modulation, using short-term HRV, and compared it among frailty statuses in the older Indian population.

2 | MATERIALS AND METHODS

2.1 | Settings and study design

This was a cross-sectional observational study, conducted on 210 older participants, aged 60 years and above with 70 participants each in frail, pre-frail, and nonfrail groups. The subjects were recruited from the outpatient department of Geriatric Medicine in a tertiary Indian hospital. Participants who were critically ill or were unable to undergo the detailed assessment (such as autonomic function test) were excluded. Participants having primary neurological disease affecting ANS, and participants with cardiac pacemaker and arrhythmias were also excluded. Written informed consent was obtained from each participant in accordance with the study protocols approved by the Institute Ethics Committee.

Demographic details, anthropometry, and clinical history were recorded for each participant. Basic activities of daily living (BADL) were assessed using Barthel's ADL instrument and even one point reduction was taken as impaired.[15] Instrumental activities of daily living (IADL) using Lawton's IADL instrument were recorded with appropriate sex modification and similarly, reduction in even one point was taken as impaired.[16] Depression was evaluated using the Geriatric Depression Scale (GDS)–a 15-item questionnaire and a score ≥5 was taken as the cut-off for depression.[17] Cognition was assessed using the Hindi Mental State Examination and a cut-off of ≤23 was used to define cognitive impairment.[18]

2.2 | Frailty assessment

Frailty was assessed using the deficit accumulation model. A questionnaire with 36 health-related variables was used and the number of positive responses was noted. The frailty index (FI) was calculated by dividing the number of positive responses by 36 (total number of variables). For evaluation of the level of frailty, three groups were devised from the continuously distributed FI using two cut points. People with three or fewer (of 36) deficits were considered to be nonfrail (FI ≤ 0.08), whereas those with nine or more deficits (FI ≥ 0.25) were considered to be frail. People with four to eight deficits, therefore, correspond to the intermediate (pre-frail) group.[19–22]

2.3 | Assessment of autonomic activity

A short-term HRV of 5 min duration was recorded.

2.3.1 | Prerecording procedure

HRV test was performed between 2:00 p.m. and 4:00 p.m. in the Autonomic Function Laboratory, Department of Physiology of the same tertiary care hospital. The room temperature was maintained around 22–24°C. The laboratory was devoid of bright colors, sounds, and bright light. The patients were instructed to wear loose clothes, to take light meals 2 h before the test, and refrain from tea, coffee, or any other beverages in the 24 h before the test. Each subject was requested to empty her/his urinary bladder before the start of the test. After reaching the laboratory, each participant was asked to lie down quietly for 15 min, and standard ECG Limb electrodes were attached.

2.3.2 | Assessment of HRV

HRV is a beat-to-beat variation in heart rate (i.e. in R-R intervals on ECG) under resting conditions which quantifies autonomic drive to the myocardium. Standard ECG limb electrodes were applied and 5 min of ECG was recorded as per the guidelines.[23–26] Subjects were asked to lie down quietly for 15 min and close their eyes, avoid talking, moving heads, legs, and body, coughing, and sleeping during ECG recording. ECG analog signals were acquired on the computer for 5 min using the National Instruments (NI) Data Acquisition Card and the software (HRV soft version 1.1) after the subject had rested for 15 min. R-R interval computed from this digitized ECG was analyzed using HRV soft version 1.1 (built using the LabView software from Texas Instruments, USA) validated with Kubios HRV version 2.0, Department of Physics, University of Kuopio, Finland, and Nervokard aHRV 12.0.0. (Medistar Inc., Slovenia).[27] R waves were detected and R-R intervals were plotted against time to obtain a tachogram. Abnormal beats were identified and dealt with adequately, whereas patients having recordings with a high number of artifacts including ectopic beats (>5) were excluded.[28] The normal-to-normal R-R interval was utilized to perform the computation of HRV measures from time and frequency domains as well as nonlinear methods. In the time domain analysis parameters such as SDNN (Standard deviation of the R-R intervals), SDSD (Standard deviation of differences between adjacent R-R intervals), rMSDD (root mean square of the sum of the squares of differences between adjacent R-R intervals), NN50 count (number of pairs of adjacent R-R intervals differing by more than 50 ms in the entire recording), and PNN50 count (percentage of NN50) were selected for the statistical analysis. These parameters are computed electronically based on variations in R-R interval in ECG recording and all of them are used as markers of parasympathetic activity. The spectral power density of the different component frequencies in the heart rate was carried out by the fast Fourier transform (FFT). The power spectrum can be divided into three frequency bands of very low frequency (VLF) 0.003–0.04 Hz, low frequency (LF) 0.04–0.15 Hz, and high frequency (HF) 0.15–0.4 Hz. In the nonlinear method, the R-R interval was analyzed using a Poincare plot which is a scatter plot of the current R-R interval against the R-R interval immediately preceding it (R-Rn vs. R-R$n+1$). SD1 (width of the ellipse on Poincare plot), SD2 (length of the ellipse on Poincare plot), and SD1/SD2 ratio were selected for analysis in the nonlinear method. HF power and SD1 indicate parasympathetic influence, whereas LF power and SD2 are indicative of sympathetic influences. For measuring balance between parasympathetic and sympathetic arms, ratios such as LF/HF and SD1/SD2 are used.

2.4 | Statistical analysis

Data were analyzed using STATA version 14. Descriptive statistics were summarized by frequency, mean, standard deviation, median, and range as appropriate. Categorical variables were compared using Chi-square/Fisher's exact test, whereas Spearman's was used for correlation between two continuous variables. Continuous variables following normal distribution were compared between three groups using one-way ANOVA followed with Bonferroni correction and those variables not following normal distribution were compared with the Kruskal–Wallis test followed by multiple comparisons using the Dunn test with Bonferroni correction. A $p \leq 0.05$ was considered statistically significant.

3 | RESULTS

Table 1 provides information about the characteristics and functional assessment of the study population. A total of 210 participants (70 each in frail, pre-frail, and non-frail groups) were recruited. The mean age of the study population was 69.93 ± 5.12 years. As shown in Table 1, there was no significant difference in mean age across the non-frail, pre-frail, and frail groups. Both males and females were equally distributed across all three groups with no statistically significant difference between them. As expected, there was a significantly higher number of participants with hypertension and type 2 diabetes mellitus in the frail group compared with the pre-frail and non-frail groups. However, except statin medications use across all groups was similar. Patients having at least one episode of fall in the last year were also significantly higher in the frail group. Patients in the frail group took more time to perform the Timed Up and Go (TUG) test. They also had the lowest grip strength and gait speed compared with the patients in the pre-frail and non-frail groups. The frail group also had significantly a greater number of patients with impaired BADL and IADL. Compared with the pre-frail and non-frail groups significantly more patients were found to be depressed in the frail group.

Table 2 shows the measures of HRV in frail, pre-frail, and non-frail groups. The measure of total HRV such as time domain parameters (SDNN, SDSD, rMSSD, NN50, and pNN50) was significantly lower in the frail group, as well as HF power and SD1 were also significantly lower in the frail group compared with pre-frail and non-frail group, suggesting decreased parasympathetic drive at rest in the frail group. LF power and SD2 were significantly lower in the frail group compared with the pre-frail and non-frail group, suggestive of decreased sympathetic drive at rest in frail patients. There was significantly lower total power in the frail group compared with the pre-frail and non-frail groups, suggestive of decreased total autonomic drive at rest in frail patients. FI was found to have a significant negative correlation with time domain parameters of HRV (NN50, pNN50, SDNN, SDSD, rMSSD), Frequency domain parameters (LF power and HF power), and nonlinear parameters of HRV (SD1 and SD2) (Table 3).

4 | DISCUSSION

The integration and proper functioning of various physiological systems are essential for maintaining overall health and well-being

TABLE 1 Characteristics and functional assessment of the study population.

Variables		Total ($n=210$)	Nonfrail ($n=70$)	Pre-frail ($n=70$)	Frail ($n=70$)	*P*-Value
Age (years) (Mean ± SD)		69.93 ± 5.12	69.21 ± 4.00	70.23 ± 5.60	70.34 ± 5.58	0.357
Sex	Male	140 (66.67%)	48 (68.57%)	47 (67.14%)	45 (64.29%)	0.861
	Female	70 (33.33%)	22 (31.43%)	23 (32.86%)	25 (35.71%)	
Body mass index (kg/m^2) (*Mean ± SD*)		23.52 ± 4.20	23.49 ± 3.98	23.73 ± 4.19	23.35 ± 4.48	0.864
Current smoker		14 (6.66%)	8 (11.43%)	4 (5.71%)	2 (2.86%)	0.148
Comorbidities						
Hypertension		79 (37.61%)	34 (48.57%)	37 (52.86%)	48 (68.57%)	0.042
Diabetes mellitus		61 (29.04%)	5 (7.14%)	21 (30.00%)	35 (50.00%)	<0.001
Chronic obstructive airway disease		31 (14.76%)	7 (10.00%)	15 (21.43%)	9 (12.86%)	0.140
Coronary artery disease		17 (8.09%)	3 (4.29%)	4 (5.71%)	10 (14.29%)	0.080
Cerebrovascular disease		8 (3.80%)	1 (1.43%)	2 (2.86%)	5 (7.14%)	0.282
History of nonaccidental fall		24 (11.42%)	3 (4.29%)	6 (8.57%)	15 (21.43%)	0.006
Functional Assessment						
TUG score (s) (*Mean ± SD*)		13 ± 4.42	10.17 ± 1.83	12.26 ± 2.56	16.59 ± 5.25	<0.001
Grip strength (kg) (*Mean ± SD*)		24.79 ± 7.55	29.07 ± 7.19	25.79 ± 6.75	19.52 ± 5.25	<0.001
Gait speed [time taken to walk 15 feet in seconds] (*Mean ± SD*)		5.43 ± 1.83	4.22 ± 0.70	5.13 ± 1.17	6.93 ± 2.10	<0.001
Impaired IADL		74 (35.24%)	4 (5.71%)	22 (31.43%)	48 (68.57%)	<0.001
Impaired BADL		49 (23.33%)	2 (2.86%)	8 (11.43%)	39 (55.71%)	<0.001
Impaired GDS		75 (35.71%)	7 (10.00%)	24 (34.29%)	44 (62.86%)	<0.001

TABLE 2 Analysis of heart rate variability (HRV) across frailty status.

HRV variables	Nonfrail ($n=70$) [Mean ± SD or Median (range)]	Pre-frail ($n=70$) [Mean ± SD or Median (range)]	Frail ($n=70$) [Mean ± SD or Median (range)]	*P*-Value
Mean R-R interval in milliseconds (ms)	818.57 ± 144.29	825.61 ± 137.59	745.95 ± 119.51	<0.001
Time domain parameters				
NN50	3.5 (0–243)	0.5 (0–72)	0 (0–76)	<0.001
pNN50	1.06 (0–64.29)	0.11 (0–21.2)	0 (0–27.64)	<0.001
SDNN (ms)	29.42 ± 13.61	21.14 ± 7.16	14.73 ± 6.62	<0.001
SDSD (ms)	20.84 (2.9–87.26)	12.4 (3.55–39.33)	8.51 (2.32–43.9)	<0.001
rMSSD (ms)	20.81 (2.89–87.14)	12.38 (3.55–39.26)	8.5 (2.32–43.82)	<0.001
Frequency domain parameters				
LF (ms^2)	164.765 (17.83–1490.72)	97.84 (11.13–590.4)	59.675 (2.48–394.87)	<0.001
HF (ms^2)	139.53 (3–4062.29)	71.185 (2.92–493.91)	35.215 (2.55–528.06)	<0.001
LF/HF	1.09 (0.08–18.02)	1.28 (0.17–15.39)	1.46 (0.13–6.20)	0.294
Nonlinear parameters				
SD1	14.47 (2.04–61.35)	8.74 (2.51–27.86)	6.02 (1.64–31.07)	<0.001
SD2	41.25 ± 18.95	29.52 ± 9.99	20.62 ± 9.35	<0.001
SD1/SD2	0.39 ± 0.15	0.36 ± 0.13	0.36 ± 0.11	0.218

throughout life. The loss of physiological complexity can impact health and lead to functional decline or frailty.[7,29] Frailty is thought to arise from an accelerated decline in physiological reserves over time. When this decline reaches a stage where the homeostatic mechanism starts to fail, it results in frailty.[6] This study aimed to find an association between one such homeostatic mechanism of the body which modulates cardiac autonomic function, and frailty. In our study subjects, cardiac autonomic activity (tone) was

TABLE 3 Correlation of frailty index (FI) with heart rate variability (HRV) parameters.

HRV variables	Correlation coefficient	*P*-Value
NN50	−0.3445	<0.001
pNN50	−0.3472	<0.001
SDNN	−0.5082	<0.001
SDSD	−0.4344	<0.001
RMSDD	−0.4345	<0.001
LF	−0.4519	<0.001
HF	−0.4306	<0.001
LF/HF	0.0786	0.296
SD1	−0.4329	<0.001
SD2	−0.5119	<0.001
SD1/SD2	−0.0718	0.301

assessed by measuring short-term HRV at rest and was analyzed in terms of time domain, frequency domain, and nonlinear methods. Frailty was measured with the FI based on the deficit accumulation model.[19–22]

Our study indicates that both cardiac parasympathetic and sympathetic modulation at rest is significantly lower in the frail group (based on FI) compared with pre-frail and non-frail groups ($p < 0.05$). Sympatho-vagal balance as measured by LF/HF and SD1/SD2 didn't show any statistical significance. This may suggest that, although both sympathetic and parasympathetic drive decreases in frail patients, the balance between both components of autonomic function remains intact. Furthermore, all the parameters of HRV except LF/HF and SD1/SD2 were negatively correlated with the frailty index, which indicates that autonomic modulation in an individual decreases as the patient becomes frailer.

Various studies have shown that HRV decreases with aging.[30,31] These studies demonstrated that HRV decreases with aging, showing an early decline of cardiac parasympathetic modulation as reflected by a rapid reduction in the pNN50 index. On the other hand, rMSSD, which is another index of cardiac parasympathetic modulation, declines more gradually over time. Moreover, they also demonstrated differences in HRV indices among men and women. However, only a few studies have investigated the relationship between frailty and HRV,[28,32] and in general, reported that frailty is associated with impaired cardiac autonomic modulation. From the secondary analysis of baseline data from a subset of older women in the Women's Health and Aging Study (WHAS; 1992–1995), Chaves et al.[32] concluded that Median $ApEN_{HR}$ (Approximate entropy for HRV) was lower in frail subjects, suggesting lower physiological complexity in frail patients and thus lower autonomic modulation in them. Lower $ApEN_{HR}$ was associated with a higher likelihood of frailty than higher $ApEN_{HR}$. They also found that subjects who had lower ApEnHR were twice as likely to be classified as frail as those without lower ApEnHR. Frailty was also found to be associated with lower levels of traditional time domain and frequency domain indices of HRV. Specifically, all indices of lower HRV were associated with a higher probability of frailty ($p < 0.05$), except HF power and rMSSD. However, we found both HF power and rMSSD also to be significantly lower in frail subjects.

In a study conducted on older women, Katayama et al.[28] suggested a decreased power in the HF band (absolute values) in the frail group compared with the non-frail group, indicating decreased parasympathetic drive at rest, which is consistent with the observations of our study. However, no significant difference was found in terms of SDNN and rMSSD across all groups, which does not align with our study where all the time domain parameters of HRV including SDNN and rMSSD were significantly lower in frail subjects compared with other groups. They observed higher sympathetic and lower parasympathetic modulation in frail when compared with non-frail and pre-frail groups ($p < 0.05$) as demonstrated by frequency domain indices. The frail group showed an increased LF/HF ratio (indicating altered sympathovagal balance toward higher sympathetic modulation) when compared with the non-frail and pre-frail groups. A similar trend was seen in our study; however, it was not statistically significant.

This study has tried to identify a potential noninvasive approach to assess frailty by measuring cardiac autonomic modulation in terms of short-term HRV. Although Long-term HRV analysis can predict adverse health outcomes including all-cause mortality, it is a cumbersome and nonpractical approach due to its high cost and time constraints. Short-term HRV analysis offers a more practical approach. As frailty is defined as an impairment in interrelated physiological systems, by identifying decreasing autonomic modulation with frailty, our study has provided further evidence regarding its pathophysiological basis.[6,33,34] However, differing observations found with respect to the aforementioned studies and the current study suggest that there is still a lack of understanding in terms of how to utilize HRV when assessing frailty.

This study has tried to assess short-term HRV by all three methods of HRV analysis including time domain, frequency domain, and nonlinear analysis methods among frailty statuses. It could help us understand how cardiac autonomic modulation can be studied as a surrogate marker of frailty using short-term HRV measures. This study had an adequate representation of both male and female subjects across all groups. Comorbidities such as coronary artery disease and cerebrovascular disease, and Medications such as beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin receptor blockers that can directly affect autonomic function were balanced among all three groups. Nevertheless, this study is not devoid of limitations. First, it was a cross-sectional study. Therefore, we will not be able to derive a causal relationship between autonomic function impairment and frailty. Further, comorbidities like diabetes mellitus which can directly affect autonomic function were higher in subjects in the frail group. However, comorbidities are part of frailty so it has to be read with a matter of caution. To circumvent this issue further studies using the phenotypic model[5] of frailty can be planned. Lastly, patients using medication that can indirectly affect autonomic function such as oral hypoglycemic agents and lipid-lowering drugs were not balanced among all three groups. However,

it is difficult to exclude patients not using such medications due to a high prevalence of comorbidities requiring these medications among the older population.

5 | CONCLUSION

Frailty is significantly associated with a decrease in cardiac autonomic modulation. Both sympathetic as well as parasympathetic activity decreases with increasing frailty status, although the balance between them can still be intact. Short-term HRV analysis provides a measure of this variability in cardiac autonomic modulation and has the potential to be used as a quick and noninvasive biomarker for assessing frailty in older adults. However, further studies with larger sample sizes are needed to validate the utility of short-term HRV as a consistent and reliable biomarker for frailty.

AUTHOR CONTRIBUTIONS

All authors made a significant contribution to the work reported. All authors: Writing of paper. Gevesh Chand Dewangan: Design; data collection; statistical analysis. Sunny Singhal: Literature review; statistical analysis. Dinu S Chandran: Data collection. Maroof Ahmad Khan: Design and Statistical analysis. Aparajit Ballav Dey: Design; data collection; literature review. Avinash Chakrawarty: Design; data collection; literature review; coordination.

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The authors have nothing to report.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest in this work.

ETHICS STATEMENT

This study was approved by the institutional ethics committee of All India Institute of Medical Sciences, New Delhi (IECPG–297/07.09.2017, RT–31/28.09.2017, OT–6/29.05.2019).

INFORMED CONSENT

All the participants provided written informed consent to participate in this study.

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