ASSOCIATION BETWEEN HEART RATE RESTING STATE ENTROPY AND HEART RATE DYNAMICS AMONG HEALTHY ADULTS AND PATIENTS WITH AORTIC STENOSIS.

by

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Land Acknowledgement

We respectfully acknowledge the University of Arizona is on the land and territories of Indigenous peoples. Today, Arizona is home to 22 federally recognized tribes, with Tucson being home to the O'odham and the Yaqui. Committed to diversity and inclusion, the University strives to build sustainable relationships with sovereign Native Nations and Indigenous communities through education offerings, partnerships, and community service.

Dedication

I dedicate this study to my family and friends, who have helped me throughout this journey.

Table of Contents

List of Figures

List of Tables

ASSOCIATION BETWEEN HEART RATE RESTING STATE ENTROPY AND HEART RATE DYNAMICS IN PATIENTS WITH AORTIC STENOSIS.

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ABSTRACT

Introduction: Aortic Stenosis (AS) is a cardiovascular disease that restricts the blood flow from the left ventricle to the aorta and leads to a decline in physical activities in people with such conditions. Heart rate (HR) complexity has been implemented as a standard method to assess cardiac autonomic dysfunction in cardiovascular diseases. The HR complexity is derived from the electrocardiogram (ECG) signals while the participant rests for a minimum of five minutes. The focus of this study is to compare the HR complexity during a 5-minute resting period and the HR dynamics, which is a novel approach to measure HR changes during a 20-second physical activity among healthy young adults and older adults with AS.

Methods: Healthy young adults (controls) aged 18-30 years and older adults (>60 years) with AS were recruited for this study. HR complexity was assessed by asking the participants to sit still with no interaction or movement, and HR was recorded for 5 minutes. HR dynamics were assessed when participants performed a physical task (20 seconds baseline, 20 seconds of rapid elbow flexion with the right arm, and 30 seconds recovery). HR was recorded using an ECG sensor attached to the left side of the chest and upper rib. The multiscale entropy (MSE) method with a selected scale factor of 20 was used to measure complexity during the 20 seconds physical task using time series of intervals between the heartbeats. HR dynamics parameters included

percent change in HR during the activity and the recovery period after the arm flexion task. ANOVA models were used with the groups, age, BMI, and sex as independent and HR dynamics and the MSE values as dependent variables. Pearson correlations between MSE and HR dynamics were calculated.

Results & Discussion: A total of 70 participants were recruited for this study, including 30 healthy controls (age=21±6 years) and 40 AS patients (age=71±11 years). There was a significant difference between HR dynamics (HR increase and decrease) between controls and AS patients, mean values of 41.46% and 15.70% for HR increase (p=0.0055) and mean values of -27.04% and -13.15% for HR decrease (p=0.0007), for controls and AS patients, respectively. The Pearson correlation between the HR dynamics and the MSE data among the two groups combined showed significant associations. Results suggest that the proposed HR dynamics can provide a quicker measure of autonomic control deficits in AS.

Significance: Current findings suggest that HR outcomes obtained from a quick 20s test during physical activity can provide information on cardiac autonomic dysfunction in AS patients. AS is mainly associated with an increased risk of frailty in older adults. Frailty is a syndrome associated with low physiological reserve, which leads to muscle loss and autonomic dysfunction. Currently, there is no specific device or assessment tool available to detect frailty in AS patients. Hence, our current findings suggest that the HR dynamics outcomes obtained could provide information for assessing frailty in AS. For future investigations, we will develop an easy-to-use app on a smartwatch for identifying frailty with the use of simultaneous measures of HR dynamics and motor performance.

1. INTRODUCTION

1.1. Background of Aortic Stenosis and its Relation to the Heart Function

Aortic Stenosis (AS) is a cardiovascular disease that occurs when the aortic valve in the heart becomes narrow or obstructed and further restricts blood flow from the left ventricle to the aorta, to be transported to the rest of the body which leads to damage to the heart, serious health complications, and death. It usually progresses fast in a short time, leading to heart failure. AS condition typically increases with age; hence, as one gets older, the risk of getting diagnosed with AS is high, especially in older adults with high blood pressure that is not controlled and those with diabetes or high cholesterol (Pujari & Agasthi, 2023). AS symptoms may include chest pain, heart murmur, and heart palpitation. It can lead to problems such as arrhythmias and infection in the heart muscles from endocarditis, as well as bleeding, stroke, and blood clots, leading to cardiovascular failure. Genetic causes and certain diseases that interfere with the functioning of the aorta are known causes of crux stenosis, e.g., congenital heart disease and other infectious conditions (Carabello & Paulus, 2009). Some factors that can affect AS patients, make them more imbalanced, and increase their stressed state include hypertension, smoking, and diabetes mellitus.

1.2. Activity of the heart and its interactions as a system

The heart is an integral part of the cardiovascular system of the body as it functions to propel blood all over the body (Chizner et al., 1980). According to research, AS is one of the leading causes of sickness and death globally, and among other factors, hospitalizations due to heart failure account for a notable proportion of health expenditure (Roth et al., 2020; Kazi & Mark, 2013). Aortic stenosis (AS) is the most frequently acquired valvar ailment, with a prevalence of more than 12% in those above the age of 75 years (Osnabrugge et al., 2013). One commonly used indicator of autonomic activity is heart rate variability (HRV), defined as variations in the instantaneous heart rate or the beat-to-beat interval (Heart rate variability, 1996). According to a review by Bertson et al. (1997), the interaction between the parasympathetic and sympathetic nervous systems influences the sinoatrial node, resulting in HRV. When the nerves of the ANS are damaged, it leads to autonomic dysfunction, generally known as autonomic neuropathy. Autonomic dysfunction in aortic stenosis ranges from mild to a life-threatening situation, which leads to heart failure. It is a risk factor that may lead to sudden death in patients with severe aortic stenosis (Ambrosy et al., 2014). The interactions between the HR changes during the physical activity could measure the deterioration of the ANS during the resting state and physical activity session. (Torres-Arellano et al., 2021)

1.3. The use of non-linear analysis compared to conventional heart rate variability.

Non-linear measurements of HRV usually consist of complex interactions between humoral, hemodynamic, and electrophysiological factors as well as those controlled by the autonomic and central nervous systems. According to research, these methods are effective tools for characterizing a variety of complex systems and provide prognostic information about patients with cardiovascular diseases such as heart failure and AS. Compared to linear metrics such as standard deviation or spectral power, nonlinear analysis techniques such as the entropy measures can provide a more comprehensive understanding of the nonlinear regulatory mechanisms controlling HRV. HRV data may contain hidden patterns, structure, and dynamics that are not always visible when using linear analysis techniques. This includes finding fractal patterns, or nonlinear interactions among physiological processes and variations in heart rate. Non-linear analysis can reveal early warning signs of pathological alterations in cardiovascular function. Autonomic dysfunction, a higher risk of mortality, and several cardiovascular diseases have all been linked to abnormalities in nonlinear measures of HRV. In this study, the non- linear analysis used was entropy measures. Measures of entropy shed light on the resilience, predictability, and stability of systems. Having high entropy values indicate a greater complexity and unpredictability, whereas more regular and predictable behavior is suggested by low entropy values. The use of entropy measures to evaluate the dynamics and reaction to the disturbances of the system, this data is helpful.

1.4. Assessment of Cardiac Autonomic Dysfunction

For this study, the heart rate complexity was measured during a rest period of 5 minutes by recording the heart rate with an ECG device. The heart rate dynamics were measured during physical activity of flexion and extension of the elbow for 20 seconds to show the decrease and increase in heart rate. The changes in the heart rate were also measured during the 6-minute walking distance test (6 MWD). In addition, we introduced the use of the Multiscale entropy method, which considers the various time scales in the heart rate at a scale of 20 to measure the HR complexity and create a correlation of the HR dynamics between the healthy young adults and the older adults with aortic stenosis, considering their HR complexity at the resting state and the physical activity phase (Humeau-Heurtier, 2020).

1.5. Hypothesis/Significance of the study

The study's primary goal is to compare the heart rate complexity during the 5-minute rest period and the heart rate dynamics during the 20s physical activity in healthy young adults and older adults with Aortic Stenosis. The hypothesis for the study was that the correlation between the heart dynamics (HR increase and decrease) among non-AS and AS patients proposed that the HR outcomes can be a good predictor of AS condition in older adults. The second hypothesis obtained from the study suggested that the HR outcomes achieved during the 20s physical task can provide more knowledge on autonomic dysfunction in AS patients (Shafie et al., 2018; Berntson, 1997).

2. METHODS

2.1. Criteria for recruitment

A total of 74 participants were recruited: healthy young adults and older adults with AS. The controls consisted of healthy young adults between 18-30 years old, whilst the patients were older adults above 64. The healthy adults were mainly recruited from the university, and the older adults were recruited from the Banner University Pacemaker clinic between August 2021 and July 2023. The inclusion criteria for selecting the older adults were: i) must be 65 years and older, ii) must be able to walk at least 30ft. The exclusion criteria for the selection of older adults were: i) being diagnosed with diseases that directly affect the heart rate with severe motor disorders such as stroke; ii) being diagnosed with a progressive disease that may lead to death within six months; iii) usage of β-blockers or medication that influence HR; iv) diagnosed with diseases that affect the HR directly. The University of Arizona Review Board approved the study, and written consent was made according to the principles expressed in the Declaration of Helsinki (World Medical Association, 2013).

2.2. Clinical Measures

The clinical measures that were collected for the healthy young adults include: 1) comorbidity based on the Charlson Comorbidity Score (CCI) (Folstein et al., 1975); 2) depression using Patient Health Questionnaire (PHQ-9) (Folstein et al., 1975); and for AS patients, 1) MMSE and Montreal Cognitive Assessment (MoCA) for cognition (World Medical Association, 2013; Fieo et al., 2013). 2)The quality of life (QoL) is assessed using the Kansas City Cardiomyopathy

Questionnaire (KCCQ) (Nasreddine et al., 2005). Because clinical measures may impact cardiovascular system performance and physical activity, they were considered adjusting variables in the statistical analysis for both groups when they showed a significant association with frailty (Spitzer et al., 2019).

2.3. Data Acquisition

During the data collection, the participants were made to sit still, and data was collected. The raw data was extracted by attaching electrodes of an Electrocardiogram (ECG) monitoring device to measure the HR during the 5-minute resting period and 20s physical task. Two tri-axial gyroscopes were placed on the participant's right upper arm and right wrist to take the motor data during the physical task of the 20s. To return to their regular resting state, participants were instructed to sit in a chair and rest for two minutes. After that, participants were asked to use their right arm to complete the UEF task, which involved flexion-extension of their elbow as quickly as possible for 20 seconds. Participants were made to rest on the chair for an additional two minutes after the UEF task. From our previous studies, we have demonstrated that the left and right hands yield similar UEF results. To familiarize themselves with the protocol, participants performed the UEF test on their non-dominant arms before the test. Participants were explained the protocol and, using the same verbal cues, were urged to complete the task as quickly as possible just once, before flexion of the elbow. Wearable motion sensors (sampling frequency=100 Hz, triaxial gyroscope sensors, BioSensics LLC, Cambridge, MA) were employed to gauge the motion of the upper and forearms, and the angular velocity of the elbow. The gyroscope angular velocity data were filtered using a first-order high-pass butter-worth filter, which had a 2.5 Hz cutoff. Elbow flexion cycles were identified after the angular velocity signal's maximums and minimums were found. The following factors were used to evaluate motor performance: 1) range of motion based on elbow flexion speed; 2) flexibility based on range of motion; 3) upper-extremity muscle strength based on weakness; 4) speed variability and motor accuracy; 5) fatigue based on speed decrease during the 20-second task; and 6) number of flexion cycles. Each of those features was given a sub-score, which was previously determined using multivariable ordinal logistic models. The dependent variable was the Fried frailty categories, while the independent variables were UEF parameters and demographic data).

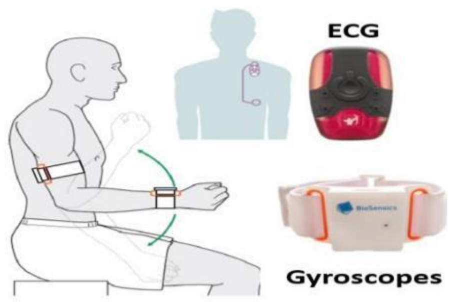
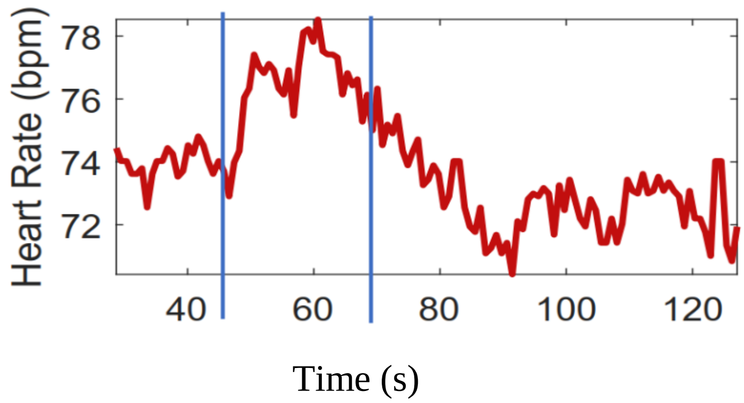


Figure 1: Wearable devices (gyroscopes) to obtain angular velocity and ECG during the UEF physical task.

2.4. HR dynamics measurement

A wearable ECG device (360° eMotion Faros, Mega Electronics, Kuopio, Finland; ECG sampling frequency=1000 Hz and accelerometer sampling frequency=100 Hz; Figure 1A) with two electrodes and one built-in accelerometer was used to record HR. One ECG electrode was placed on the upper mid-thorax, and the other was placed on the inferior to the left rib. The movement artifacts from the UEF test with the right arm would be reduced if the electrodes were placed on the left chest. The participants measured and compared the HR dynamics during rest and physical tasks (20s baseline, 20s rapid elbow flexion with the right arm, 30s recovery). The HR dynamics include the time to reach maximum peak and recovery. RR intervals, or the QRS signal's successive R peaks, were calculated using the Pan-Tompkins algorithm. The HR percentage increase and decrease during physical activity and recovery period were compared among the two groups (Brindle et al., 2016).



Heart Rate variability during the physical task

2.5. Multiscale Entropy

To compare the HR percentage increase and percentage decrease among the two groups during physical activity the multiscale sample entropy method was incorporated. Multiscale sample entropy provides differences in fluctuations over a range of time scales between groups at multiple time scales (Humeau-Heurtier, 2020). MSE method assesses the heart rate variability (HRV) signals in patients and identifies anomalies in autonomic nervous system activity.

The MSE approach comprises a coarse-graining method representing the different time scales' dynamics. The formula below was used to obtain the MSE values.

$$yj^{(\tau)} = \frac{1}{\tau} \sum_{i=(j-1)\tau+1}^{j\tau} xi$$

where τ represents the scale factor and $1 \leq j \leq N/\tau$.

The length of each coarse-grained time series is N/τ.

To gain the MSE values, the signal's entropy is calculated at different temporal scaled by dividing the original time series into non- overlapping segments of varying lengths. The main reason of using the MSE approach over other methods in this analysis, is to know the time scale of relevance in the time series, i.e. considering the time scales of each variation in the signal rather than the signal in general. The signal entropy is calculated using a sample entropy, and these measures quantify the use degree of variations in the signal. The sample entropy was obtained by using the formula below.

$$SampEn(r) = -In\left[\frac{Cm+1(r)}{Cm(r)}\right]$$

$$where,\ C^{m}(r) = (N-m+1)^{-1}\sum_{i=1}^{N-m+1} Cm(r).$$

where N is the data length, m=2, r=0.2 (22)

The time series of intervals between heartbeats was analyzed, and the MSE Scale factor of 20 was used for the analysis. A scale factor of 20 was chosen because according to researchers, a higher scale factor gives a better MSE analyses and helps to determine the resolution at which the time series is decomposed into segments. With a sampling frequency of 10Hz, a correlation was created between the HR dynamics (percentage increase and decrease) of healthy young adults and older adults with AS. After the sample entropy is calculated for each time scale, a multiscale entropy profile is generated, which represents the complexity of the signal when changing across different time scales and is plotted versus the MSE Scale. The diagram below shows the results obtained from the multiscale scale entropy of Scale 20 comparing healthy young and older adults with AS.

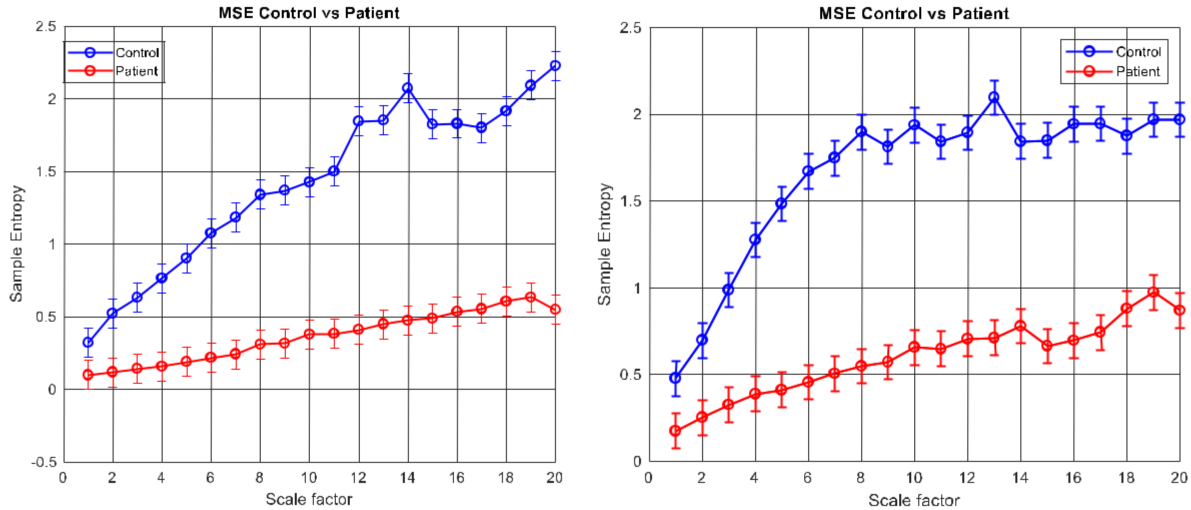


Figure 2: Multiscale Entropy Analysis of Scale 20 between control and Patients.

2.6. Statistical Analysis

The differences between the two groups in all continuous parameters of the clinical measures, HR parameters, MSE parameters, and demographics except sex were assessed using analysis of variance (ANOVA) models. Chi-square (χ^2) tests were used to assess differences in sex among the two groups. First, Pearson correlation tests were investigated for every participant's HR parameter to evaluate the relationship between HR dynamics during physical activity and HR parameters at rest. This step involved investigating the HR percentage increase and decrease for both groups. The HR dynamics and MSE parameters between the two groups were also compared using the multivariable ANOVA models, where age, sex, and BMI were considered as adjusting variables, and the control and AS patients (two groups) were considered dependent variables. The statistical analysis was performed using JMP® Pro 16.1.

3. RESULTS

3.1. Participants and clinical measures

A total of 70 participants were recruited for this study, including 30 healthy controls (age=21±6 years) and 40 AS patients (age=71±11 years). There were significant differences in age, height, and weight between the controls and patients; hence, the statistical analysis was done around these two groups. A summary of the demographics is illustrated in Table 1.

Table 1: Demographic Table

Parameters	Control (n=30)	AS Patients (n=40)	Combined participants	P-value
Age Range	21.967 (18-28)	71.76 (56-89)	46.863	<0.0001
Sex (%)	46% (M) / 54%(F)	53% (M) / 47% (F)	49.5% (M) /50.5% (F)	0.4981
Height, cm (SD)	166.31 (11.17)	169.74 (10.31)	168.02 (10.74)	0.81
Weight, kg (S.D.)	72.30(16.85)	79.75 (21.32)	76.02 (19.08)	0.26
BMI	26.12 (5.63)	27.46 (5.83)	26.79 (5.73)	0.29

3.2. Comparison of healthy participants vs AS patients

HR increase vs HR decrease (HR Dynamics)

All HR change parameters are recorded in Table 2 below. There was a significant difference or effect in AS patients concerning the HR percentage increase and decrease ($p<0.01$). AS participants showed lower or worse HR changes during the physical activity compared to the control group. During MSE, parameters showed significant results across both groups concerning the HR percentage increase and decrease ($p<0.01$). The study found a notable difference in heart rate (HR) dynamics between control subjects and patients with (AS). The average HR increase recorded a statistically significant difference in both groups(p=0.0055). The average HR decrease also showed a statistically significant difference in both groups (p=0.0007).

Table 2: HR complexity for resting state entropy vs HR dynamics during physical activity

HR Parameters	**Controls, Mean**	**AS Patients**	**P-value**
HR Rest, Mean (SD)	76.20 (15.34)	70.45 (14.27)	0.24 (0.30)
Recovery Time, (SD)	14.04 (5.83)	26.20 (9.54)	<0.0001* (1.73)
HR Increase (%)	41.46(28.22)	15.70 (7.88)	0.0055 (0.91)
HR Decrease (%)	-27.04 (11.84)	-13.15 (6.39)	0.0007 (0.66)

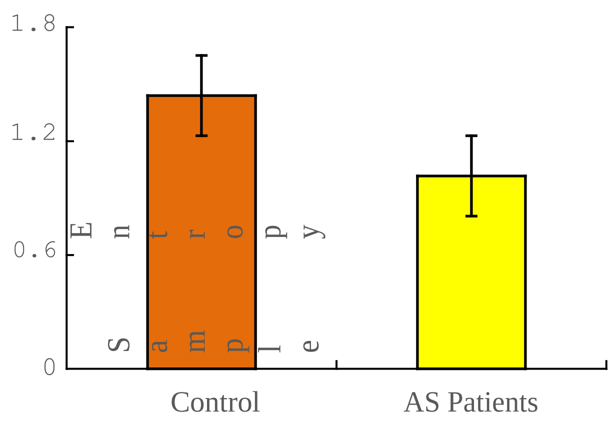


Figure 3: HR Resting State Entropy between Controls and Patients.

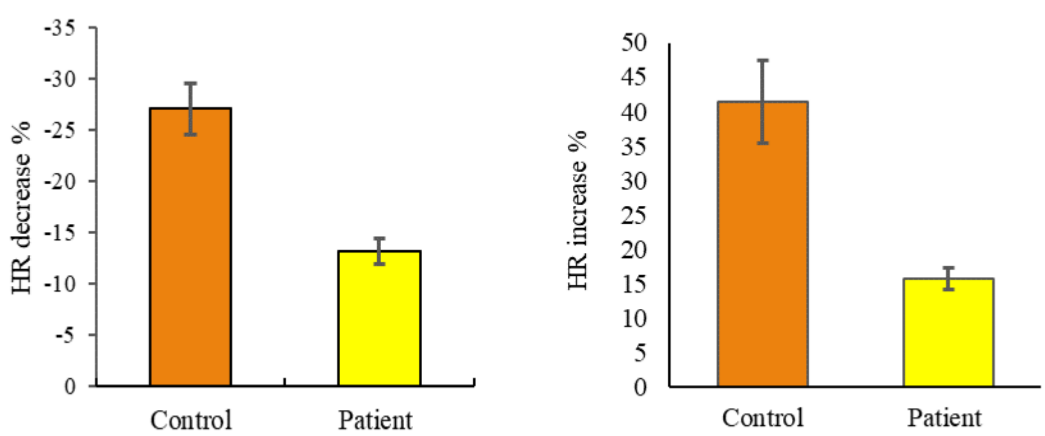


Figure 4: Percentage of HR increase and decrease between Controls and AS Patients during physical activity.

3.2. MSE analysis

A significant correlation was observed between HR dynamics and Multiscale Entropy (MSE) data across both groups ($p<0.0019$), with correlation coefficients ranging from 0.2 to 0.37. These findings suggest that HR dynamics offer a faster way to detect deficits in autonomic control in AS patients. We observed that the entropy values assigned to time series for the healthy group and AS subjects for scale one, typically used by traditional single-scale methods, were indistinguishable. The healthy subjects have the highest entropy values.

Contrary to the outcomes of the conventional Sample entropy (SampEn) algorithms, healthy young subjects are assigned the highest entropy values for all scales except the first one, indicating that healthy dynamics are the most complex (Valencia et al., 2008). Despite this, there is a significant overlap between the SampEn values for these two groups at larger time scales. This indicates that Multiscale Entropy (MSE) characteristics other than absolute values may be necessary for distinguishing between these groups (Costa & Healey, 2003).

From the results obtained in the study, the control group showed a higher MSE values compared to the AS patients' group across the 20 scale factors. In the context of MSE, a higher entropy value shows more variability in the tie series data, hence the control groups physiological signals appear to have more variations than the AS patients' group with low entropy values. The differences between the two groups can be associated with their health assessments or any disease diagnosis. Most often, a decrease in the physiological variations in the signal of an individual is associated with aging and a diagnosed disease, hence a lower complexity in the patient group indicates a health complication or a health issue.

Table 3: Comparison of MSE values between Controls and AS Patients.

Parameter	Control – Mean (S.D.)	AS Patients – Mean (S.D.)	P-value (Effect size)
MSE 2	0.58 (0.09)	0.46 (0.18)	0.0322
MSE 4	0.99 (0.23)	0.77 (0.34)	0.0469
MSE 6	1.35 (0.28)	1.02 (0.44)	0.0183
MSE 8	1.60 (0.32)	1.21 (0.50)	0.0110
MSE 10	1.79 (0.35)	1.23 (0.46)	0.0006
MSE 12	1.92 (0.45)	1.27 (0.47)	0.0007
MSE 14	1.81 (0.38)	1.31 (0.61)	0.0293
MSE 16	1.83 (0.29)	1.37 (0.51)	0.0107
MSE 18	1.99 (0.39)	1.31 (0.40)	<0.0001
MSE 20	1.87 (0.39)	1.35 (0.40)	0.0014*

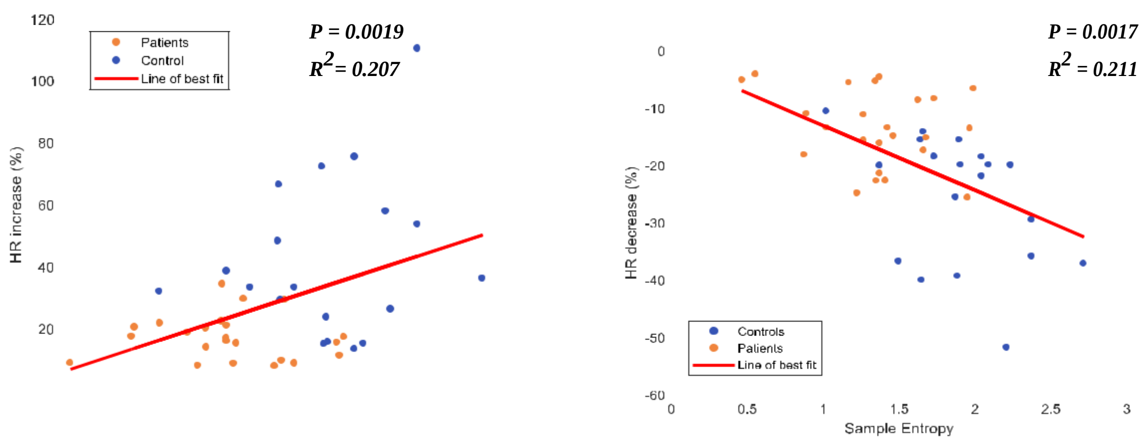


Figure 5: Correlation between HR percentage change and Sample Entropy.

4. DISCUSSIONS

4.1. Effect of HR Dynamics

As observed from the study, there were significant differences in HR changes among the two groups during physical activity and after recovery. In previous research, HRV has been suggested as a vital sign and used to evaluate ANS dysfunction (Parvenah S. et al 2015). Our current research has revealed several HR dynamics parameters, such as significant higher HR changes during and after physical activity and a significant slower HR response to the physical task, that may be used to evaluate cardiac autonomic dysfunction caused by aortic stenosis.

During physical activity, the HR increases and later reduces during the recovery period from the activity. The results showed a significant association between heart rate dynamics and resting-state HR complexity, suggesting that a quick 20-second test can help geriatricians provide information regarding cardiac dysfunction in older adults with aortic stenosis. The correlation we obtained between the Heart rate percentage increase and decrease among the healthy young adults and older adults with AS also showed significant results in both groups, suggesting that proposed HR outcomes can predict the AS condition (Metelka, 2014). In comparison of both groups, AS participants in our study had noticeably larger changes in HR during both physical activity and resting period (Table 3). The ANS's reaction to a higher cardiac oxygen demand was identified as the cause of the higher HR change in AS (Grimard BH et al) Additional research indicates that the quick increase in HR in AS patients is a compensatory mechanism to preserve cardiac output (Chambers JB, 2019).

We also noticed that the inability to maintain heart rate while at rest can put AS patients in a more unbalanced and stressed state, making it difficult for them to react to further stress, such as moving their arms. We found higher mean HR during resting among AS participants compared to non-frails, which is non-significant but confirms this theory (Toosizadeh, 2022).

4.2.Effect of MSE Analysis

Previous research using MSE demonstrates that aging and disease lead to a decline in complexity. However, time series derived from subjects with AS and subjects in good health might not be distinguished using conventional single-scale entropy-based measures. On the other hand, the MSE method shows that young, healthy subjects have the highest entropy values for larger time scales. Therefore, the idea that young, healthy systems are the most complex and adaptable is consistent with MSE results. Additionally, we have demonstrated how an automatic classification algorithm can distinguish between subjects with AS and young, healthy individuals based on the distinctive MSE profile curves. From the results, we investigated that high accuracy was still attained in the two class cases, indicating that testing on larger data sets is warranted to evaluate clinical applicability further. The MSE method discriminates between time series produced by various mechanisms. It can also be used with multiple other physical and physiological time series.

4.3. Limitations and Future Findings

The study encountered several limitations that could be considered for future research studies. There was a limited number of sample sizes for participants during the study, for both the healthy adults and AS patients, but most especially the AS patients. If the number of healthy adults and AS patients was increased, we would have more data to compare for a much better result. For our future research there must be a higher recruitment of older adults with high rate of

AS to gain more results on the AS patients. Secondly, for the MSE method to yield accurate figures for the entropy measure on each scale, there must be enough data for analysis. Hence, for future research there should be a larger data set and we could analyze more correlations of HR in the MSE analysis to gain more data points for accuracy.

For future research findings the results we obtained will further be implement and developed in the technological aspect where we create an in-built app on a smartwatch with the HR dynamics measurements and MSE parameters to record and detect frailty status in both older and younger adults who visit the clinics, especially with patients with congestive heart failure and AS. This approach would reduce the workload of the physicians and help patients reduce their frequent clinic visits, especially in their old age. This will also promote telemedicine in the healthcare industry.

5. CONCLUSION

Current findings showed that the HR dynamic changes among AS patients had smaller values than the healthy patients. In conclusion, the study shows that HR dynamics during physical activity is a good determining factor for frailty status in AS patients. The MSE analysis on the HR increase and decrease among AS patients can also help determine the frailty status in AS patients and beyond. Additionally, we demonstrated that, compared to models incorporating each of these measures separately, frailty prediction may be improved by combining the MSE HR dynamics function and HR change. The suggested multimodal approach for assessing HR dynamics in AS patients will be straightforward to help the physicians in diagnosis.

5.1. Data availability

The datasets used for the current study are available from the corresponding author upon reasonable request.

5.2. Acknowledgments

This project was supported by three awards from the National Institute of Aging (NIA/NIH - Phase 2B Arizona Frailty and Falls Cohort 2R42AG032748–04, NIA/NIH - 1R21AG059202-01A1, and NIH/NIA - 1R01AG076774-01A1) and an award from NSF (NSF 2236689 – CAREER). The views represented in this work are solely the authors' responsibility and do not represent the views of NIH or NSF. We thank Allison Klatt and Sarver Heart Cerner for the data collection.

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