Original Article

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EFFECT OF AGE AND GENDER ON HEART RATE VARIABILITY IN PATIENTS WITH HEART FAILURE

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ABSTRACT

Objective: To determine the effects of age and gender on heart rate variability in patients with heart failure.

Study Design: Cross sectional analytical study.

Place and Duration of Study: Department of Clinical Cardiac Electrophysiology Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi from April 2013 to August 2013.

Material and Methods: 47 patients with the diagnosis of chronic heart failure of either sex, having age more than 19 years and with left ventricular ejection fraction equal to or less than 40 % were included in the study. All these patients underwent Holter ECG monitoring for 48 hours using DMS 300-4A and DMS 300-7A, Holter recorders. Statistical time domain measures of heart rate variability i.e. SDNN, SDNNi, SDANN, RMSSD, pNN50 were analyzed.

Results: There were 35 male (74.5%) and 12 female (25.5%) patients with mean age of 54.68±16.79 years. Mean values of SDNN, SDANN, SDNNi, RMSSD, and pNN50 were 79.96 ms, 72.26 ms, 36.60 ms, 29.94 ms and 8.85 % respectively. There was no difference of heart rate variability between males and females (p-value > 0.05). Age was negatively correlated with all the domains of heart rate variability, however, the correlation was significant only for SDNN and SDANN (p-value < 0.05).

Conclusion: Heart rate variability reduces with advancing age irrespective of the gender reflecting increased likelihood for developing ventricular arrhythmias in the predisposed patients.

Keywords: Autonomic nervous system, Heart rate variability, Heart failure.

INTRODUCTION

There is a fine interaction between sympathetic and parasympathetic activity to sustain a balanced interna[1] environment. Various methods and processes have been developed to detect the function and integrity of the sympathetic and parasympathetic systems[1]. Unstable autonomic nervous system activity is attributed as a predictor of ventricular tachyarrhythmias which may lead to sudden cardiac death. Heart Rate Variability (HRV) is considered as the most significant, accessible and non-invasive marker to evaluate equilibrium between sympathetic and parasympathetic divisions of autonomic nervous system[2]. Knowledge of heart rate variability helps in quantifying the autonomic nervous system balance which controls heart rate and rhythm. Variations in HRV are considered as reflection of heart's ability to adapt to rapidly changing internal environment in various physiological and pathological conditions. Reduced heart rate variability is associated with poor prognosis whereas increased variability is a characteristic of healthy heart[3,4]. Autonomic nervous system dynamics have been implicated in a wide range of cardiac and non-cardiac disorders[5]. HRV thus provides remarkable prognostic information in patients with heart diseases[1].

It has been documented in various studies that young healthy females have significantly reduced sympathetic activity as compared to young healthy males[4]. Thus, in a healthy adult, female gender has protective effect against development of coronary heart diseases and arrhythmias[6]. It has been established in literature that women who are younger than 50 years have higher vagal but lower sympathetic modulations of heart rate than the age-matched

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men, however these gender-related autonomic differences disappear in the elderly age group[2,7,8]. It has also been documented in studies that prognosis of heart failure is generally better in women as compared to age the matched men. Also the mortality rate in heart failure increases with advancing age[9]. In a report from the Framingham Study it has been documented that mortality rate in heart failure increased in both men and women with the advancement of age[10].

It has been documented that autonomic nervous system imbalance due to changes in geometry of the failing heart may lead to mechanical distortion of sensory nerve endings[11]. As a result, there is an abnormal increase in the firing rate at sympathetic nerve endings thus leading to electrical instability by decreasing heart rate variability consequently generating potentially lethal ventricular tachyarrhythmias. Extensive research has been carried out in the past to find out association of age and gender with electrophysiological properties of the heart[12,13]. Age and gender affect functioning of the heart by modulating autonomic nervous system and ion channels[14]. However, data regarding their effect on heart rate variability is scant. The current study was planned to investigate the effects of age and gender on heart rate variability in patients with heart failure. The study will provide a deeper understanding about electrophysiological mechanisms involved in generating heart rate variability and cardiac arrhythmias. The study may also be beneficial in providing knowledge about the age group and gender with reduced heart rate variability as the heart failure patients corresponding to these groups may be at high risk of developing ventricular arrhythmias.

MATERIAL AND METHODS

A cross sectional analytical study conducted at Armed Forces Institute of Cardiology/National Institute of Heart Diseases, Rawalpindi (AFIC/NIHD) from April 2013 to August 2013. A formal approval was obtained from Medical Ethics Committee of Army Medical College and Institutional Review Board of AFIC/NIHD before commencement of the study. Written informed consent was also attained from the patients under study. 47 patients with the diagnosis of chronic heart failure were recruited by convenience sampling. Patients from either sex, having age more than 19 years and with left ventricular ejection fraction equal to or less than 40% were included in the study. Patients who had acute myocardial infarction during the last six weeks were excluded from the study.

Patients fulfilling the inclusion criteria underwent ambulatory ECG recording for 48 hours using Holter monitors. DMS 300-4A and DMS 300-7A, Holter recorders were used in this

Table-1: Gender differences of heart rate variability indices (N=47).

HRV indices	Male	Female	*p*-value
SDNN (ms)	78.83 ± 37.43	83.25 ± 46.15	0.91
SDANN (ms)	71.00 ± 38.21	75.92 ± 47.72	0.94
SDNNi (ms)	37.14 ± 17.66	35.00 ± 19.40	0.63
RMSSD (ms)	29.91 ± 12.78	30.00 ± 14.85	0.79
pNN50 (%)	9.06 ± 8.34	8.25 ± 8.98	0.51

Table-2: Correlation of age with different indices of heart rate variability (N=47).

HRV indices	Age	
	R-value	*p*-value
SDNN	- 0.32	0.03*
SDANN	- 0.30	0.04*
SDNNi	- 0.20	0.16
RMSSD	- 0.10	0.52
pNN50	- 0.19	0.18

*p-value significant (< 0.05)

study. After 48 hours of recording, the digital ECG data were transferred from Holter recorder to the computer having compatible software. Out of three channels, the one which displayed best ECG recording and with least artifacts was selected. The whole data were manually edited with extreme care using visual checks and correction of all QRS complexes. All the erroneous beats were identified and edited from data. After editing, the Holter ECG data were analyzed for time domain HRV analysis using 'DMS serial Holter software premier 12'. The heart rate variability variables measured in time domain were SDNN (Standard deviation of all normal to normal intervals), SDNNi, SDANN (Standard deviation of the averages of normal to normal intervals in all 5 minute segments of the entire recording), RMSSD (The square root of the mean of the sum of the squares of differences between adjacent normal to normal intervals) and pNN50 (adjacent RR intervals differing by more than 50 ms).

Statistical analysis was done using IBM SPSS version 22. Mean and standard deviation were calculated for numerical variables like age and indices of heart rate variability whereas frequency and percentage were calculated for categorical variables like gender. Mann-Whitney U test was used to compare HRV indices between male and female groups. Correlation between age and different HRV indices was calculated using Pearson correlation coefficient. Alpha value was kept at 0.05 at confidence level of 95%.

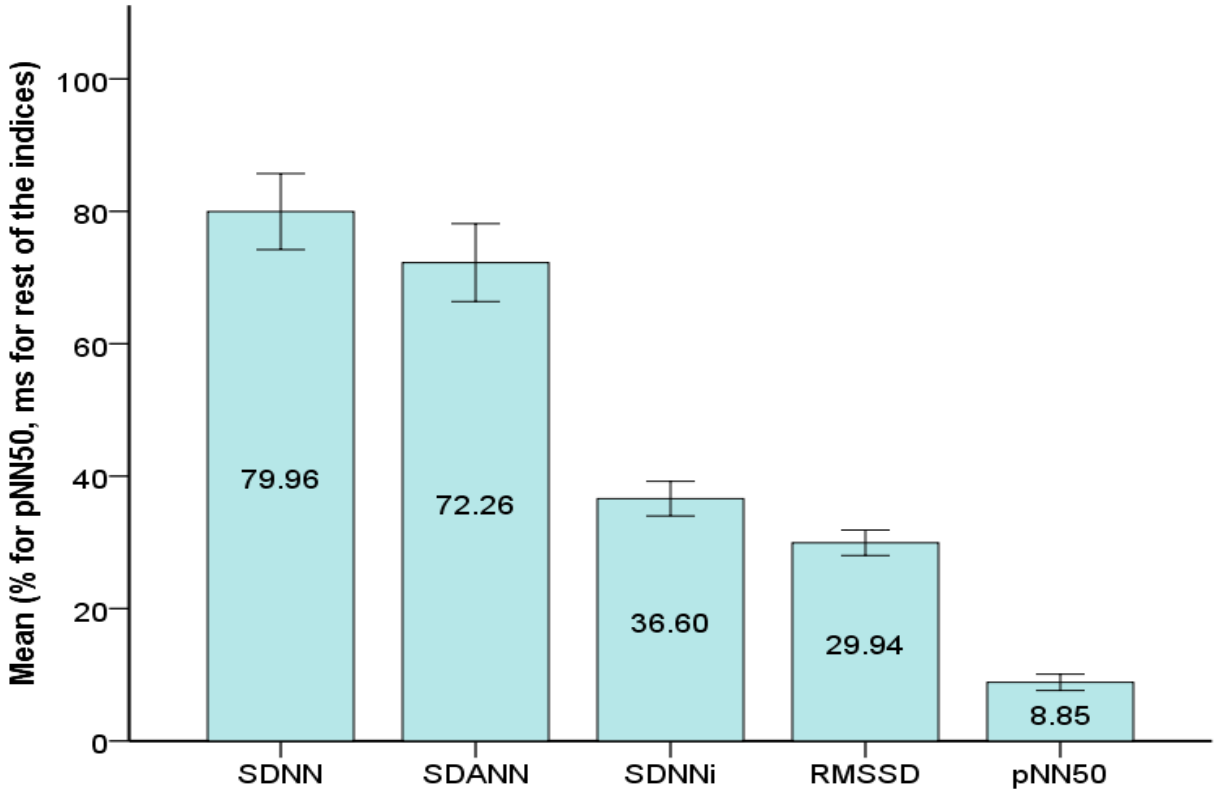

Figure-1: Mean values of heart rate variability indices (N=47).

RESULTS

There were 35 male (74.5%) and 12 female (25.5%) patients with mean age of 54.68±16.79 years. Mean values of heart rate variability in patients with heart failure are shown in Fig-1.

Comparison of heart rate variability indices between males and females is shown in table-1. The p-values, calculated by Mann-Whitney U test showed that heart rate

variability was not significantly different between males and females (*p*-value > 0.05).

Table-2 illustrates correlation of age with different indices of heart rate variability. The r-values show that age was inversely correlated with all the indices of heart rate variability, however the correlation was significant only for SDNN and SDANN (p-value < 0.05).

DISCUSSION

Results of the current study demonstrate that there was no effect of gender on heart rate variability in patients with heart failure. However, age was negatively correlated with heart rate variability indices and the correlation was significant with SDNN and SDANN. Although it is established that there are gender differences in autonomic nervous system and electrophysiological properties of heart, it seems paradoxical to report that gender does not affect heart rate variability. Current knowledge belief is that pathophysiology of heart rate variability stands on autonomic nervous system and cardiac electrophysiology. This knowledge belief appears to be contradictory with the results of current study. It seems that genesis of heart rate variability is multifaceted and some more complicated processes must be involved which might have blunted the effect of gender despite variations in the apparently underlying mechanisms. Studies have demonstrated that the effect of gender on heart rate variability disappear in the elderly age group[6]. Literature has revealed that in age strata ≥60 years there is no difference in HRV measurements between the genders[15]. The mean age of patients in the current study was 54.68 ± 16.79 years so there was possibility that gender had no impact on the variation in heart rate between males and female patients of our study. As 28 of our patients (60%) had age above 50 years, so this could again be a possible explanation for insignificant difference of heart rate variability indices between the two genders. Voss A and coworkers studied the effect of age and gender on heart rate variability in healthy subjects[16]. They reported that heart rate variability was significantly different between males and females with age below 45 years, however the difference vanished in old age groups. Females have vagal predominance as compared to males conferring stability to their heart rhythm. Some studies have reported that this beneficial effect is attributed to the female hormones[17]. After the age of menopause, due to drop in female hormones this beneficial effect is abolished which may diminish the mechanistic variations underlying heart rate variability. Another possible explanation for insignificant gender difference in heart rate variability could be the relatively small number of female patients in our study as compared to males.

Multiple factors have been implicated in reducing heart rate variability with advancing age. Out of the two divisions of autonomic nervous system, parasympathetic control is predominant over heart and it keeps the heart rate and rhythm under check. Studies have shown that with advancing age parasympathetic control of heart diminishes leading to alterations in autonomic balance.18 New balance is supposed to be in favor of sympathetic dominance which might be the underlying basis of reduced heart rate variability. Voss A and colleagues in two different studies investigated the effect of age on heart rate variability in healthy subjects[19,20]. They reported that heart rate variability reduces in all the domains with advancing age. The results are similar to our study as we also found diminished heart rate variability in all the domains with increasing age. However, in our study only the two indices SDNN and SDANN were significantly reduced with advancing age. These two indices especially SDNN correlate with overall heart rate variability which corresponds to the total power of spectral analysis. It encompasses high as well as low frequency components of heart rate variability, hence an indicator of overall functioning of the autonomic nervous system activity. Reduction in SDNN and SDANN reflects attenuation of vagal and heightened sympathetic responses and this setting may lead to initiation of many interlinked processes involved in arrhythmogenesis in the predisposed patients.

CONCLUSION

Heart rate variability reduces with advancing age irrespective of the gender reflecting increased likelihood for developing ventricular arrhythmias in the predisposed patients. This is a group of patients which needs extra medical care and supervision as ventricular arrhythmias are potentially fatal and may result in sudden cardiac death.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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