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RESEARCH ARTICLE

Alteration of heart rate variability in patients with coronary artery disease

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ABSTRACT

Background: Coronary artery disease (CAD) is one of the leading causes of mortality and morbidity in India. There is a need to identify various risk factors leading to the onset and progression of the disease. Heart rate variability (HRV) analysis is one of the emerging non-invasive techniques to identify severity and prognosis of CAD. HRV is defined as the oscillation in the interval between consecutive heartbeats as well as the oscillations between consecutive instantaneous heart rates. **Aims and Objectives:** The objective of this study is to identify the variations in HRV in patients with CAD. **Materials and Methods:** A total of 30 male patients aged 40-65 years with CAD and 30 age and sex matched healthy adults, satisfying the inclusion and exclusion criteria were enrolled in the study. **Results:** The results of our study showed a higher parasympathetic activity determined by high-frequency power (HF) in control subjects as compared to cases. Sympathetic predominance was seen in cases as determined by low-frequency power (LF). LF/HF ratio was also significantly higher in cases indicating sympathetic predominance. **Conclusion:** Sympathetic predominance with lowered parasympathetic activity observed in the cases puts them at a higher risk of adverse cardiac events. An attempt needs to be made to incorporate improvement of HRV as a modality of treatment of CAD.

KEY WORDS: Coronary Artery Disease; Heart Rate Variability; Autonomic Nervous System

INTRODUCTION

Coronary artery disease (CAD) is a major cause of mortality and morbidity worldwide. Indians are prone as a community to CAD at a much younger age and the pattern of disease is more severe and diffuse.[1-3] According to the "Global Burden of Diseases Study" in India, by the year 2020, projections for coronary heart disease mortality are 1.46 and 1.12 millions in men and women, respectively.[4] It is reported that a major part of the government exchequer has to be spent on managing subjects with CAD and serious complications arising out of the disease.[5]

The list of risk factors in the causation of the disease is long but still incomplete. One of the newly emerging risk factor is the alteration in the autonomic balance of the heart.

Heart rate variability (HRV) analysis has the potential to assess the state of the autonomic nervous system (ANS) responsible for regulating cardiac activity and overall cardiac health.[6]

HRV is a measure of the cyclic variations of beat-to-beat (RR) intervals that reflect cardiac autonomic function.[7] HRV analysis is a non-invasive and reproducible test. Decreased HRV is known to be associated with increased overall cardiac mortality, especially arrhythmic complications.[8] It is also know to predict an increased risk of all-cause mortality.[9]

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Knowledge of alterations in HRV in patients with CAD has been mainly acquired from studies in the west. It is believed that the association of these risk factors with CAD in the Indian populations needs to be ascertained. Therefore, it is necessary to undertake population-based studies to identify risk factors for causation of CAD.[10]

Thus, the aim of this study was to identify if an alteration in the balance between the sympathetic and the parasympathetic branches of the ANS does exist in CAD using HRV.

An understanding of mechanisms linking abnormal HRV to increased mortality might lead to specific therapeutic strategies that may reduce the risk of death for high-risk patients.

MATERIALS AND METHODS

The study was conducted in the Department of Cardiology and Department of Physiology, M S Ramaiah Medical College, Bengaluru.

The study protocol has been approved by the Ethical Committee of the Institution. Written informed consent was obtained from the subjects after explaining the protocol of the study in their own language. A detailed history was taken, and clinical examination was conducted.

A total of 30 male patients with treadmill test (TMT) positive/angiographically proven CAD satisfying the inclusion and exclusion criteria in the age group of 40–65 years served as cases in this case control study. The control group consisted of age, sex and anthropometrically matched, and TMT-negative subjects. Athletes, obese, alcoholics, subjects with previous history of myocardial infarction, heart failure, cardiac arrhythmias, valvular disease, congenital heart disease, implantation of pacemaker, and asthmatics were excluded from the study. The subjects were instructed to avoid rigorous exercise, intake of caffeine, and smoking 1 h before the recording.

The electrocardiography was recorded in lead-II for the duration of 5 min after a rest of 15 min by placing the electrodes in right infraclavicular, left infraclavicular, and left iliac regions. HRV was analyzed using RMS Vagus HRV software (RMS, India). Power spectral density was calculated by Fast Fourier transformation for 5 min. Low-frequency power (LF) and high-frequency power (HF) component were defined as the power between 0.04–0.15 and 0.15–0.4 Hz, respectively. The LF and HF components were expressed as normalized values (n.u.). The HRV was compared between the cases and controls.

Uniform method of recording and analysis was followed throughout the duration of the study.

Statistical Analysis

The results for each parameter are expressed as mean ± standard deviation. The student *t*-test was used to determine whether there was a statistical difference between groups in the parameters measured.

Pearson correlation coefficients were calculated to determine whether there was any correlation between the HRV parameters and age, BMI, and waist hip ratio.

$P < 0.05$ was considered as statistically significance. Data analysis was carried out using Statistical Package for Social Science Versus 10.5 package.

RESULTS

The present study was conducted with 30 cases and 30 control subjects. There was no statistically significant difference between controls and cases in the anthropometric parameter. Thus, the two groups were comparable.

In the frequency domain, the value of LF in the cases and controls was 67.95 ± 14.12 and 60.73 ± 12.38, respectively. The $P < 0.04$ indicates statistical significance. The value HF in the cases and controls was 31.98 ± 14.12 and 39.03 ± 12.54 with a $P < 0.004$ indicating statistical significance. The ratio of LF/HF in the cases and controls was 2.70 ± 1.26 and 1.82 ± 1.03, respectively, with a $P < 0.004$ indicating statistical significance. Shown in Table 2.

DISCUSSION

Morbidity and death due to CAD are assuming epidemic proportions in view of significant changes in lifestyle and food habits in India. Sedentary lifestyles associated with stress and consumption of saturated fat are blamed to be the major risk factors for CAD. Habits such as smoking and indiscriminate consumption of alcohol also contribute to degenerative changes in the blood vessel atherogenesis leading to CAD.[3] In addition to the classical risk factors, a few novel risk factors have been proposed to assess the seriousness of the CAD and also used as a tool to predict the outcome of the disease. One such novel risk factor is decreased HRV.

In our study, we have compared the HRV in the frequency domain among patients with uncomplicated CAD and normal healthy individuals. The recordings were taken between 9.30 am and 12.30 pm to avoid the influences of circadian rhythm. The cases and controls were comparable in terms of age, gender, and BMI as these factors are known to alter HRV. We found that there was a reduction in HRV in CAD evident from changes in frequency domain parameters such as LF nu, HFms^2 nu, and LF/HF ratio. In the frequency domain, a higher LF and lower HF were observed in the cases, indicating a

Table 1: Anthropometric parameters in controls and cases

Anthropometric parameters	Controls	Cases	*P* value
Age in years	54.20±6.38	53.97±6.42	t=0.02, P=0.88
Height in m	1.58±0.05	1.59±0.04	t=0.11, P=0.73
Weight in kg	62.40±6.42	64.93±6.91	t=2.16, P=0.14
BMI (kg/m^2)	24.86±2.68	25.69±2.57	t=1.48, P=0.22
Waist/hip ratio	0.88±0.05	0.88±0.87	t=0.034, P=0.85

Table 2: Comparison of HRV parameters between the cases and controls

HRV parameters	Cases *n*=30	Controls *n*=30	P value
HR beats/min	88.77±4.20	75.23±6.17	t=98.43, P<0.001
LF ms^2	51.50±44.95	45.87±35.50	t=0.290, P<0.592
HF ms^2	21.47±19.00	33.20±33.34	t=2.803, P<0.04
LF n.u	67.95±14.12	60.73±12.38	t=4.42, P<0.04
HF n.u	31.98±14.12	39.03±12.54	t=4.17, P<0.046
LF/HF ratio	2.70±1.26	1.82±1.03	t=8.79, P<0.004

HRV: Heart rate variability, LF: Low frequency power, HF: High power

higher sympathetic activity and reduced parasympathetic activity. LF/HF ratio reflects sympathovagal balance. The LF/HF ratio was significantly higher in cases when compared to the controls indicating a sympathetic predominance.

A similar alteration in HRV associated with CAD has been shown in various other studies like Hayano *et al*. who reported an impairment of vagal function in their study. However, Hayano *et al*. have included patients with previous myocardial infarction which is a confounding factor and has been avoided in our study.[11] B Wennerblom *et al*. analyzed the HRV in patients with uncomplicated CAD and found a reduction of HRV in the higher spectrum of frequencies.[5] Kunz *et al*. demonstrated that patients with CAD had a lower complexity of HRV, greater sympathetic modulation, and lower parasympathetic modulation.[12] A change in the balance between the sympathetic and the parasympathetic nervous system is associated with increased risk of arrhythmias such as ventricular fibrillation, resulting in sudden death of patients.[13-15] These deaths occur in spite of patients being on regular monitored treatment for CAD. Tsuji *et al*. have demonstrated that all-cause mortality is also higher in these individuals with reduced HRV.[9] The mechanism at play for increased mortality and morbidity is postulated to be increased sympathetic tone associated with elevated catecholamine levels that will have direct effect on vascular smooth muscle cells and influence factors promoting progress of atherosclerosis.[16] Another proposed mechanism is ischemia of the myocardial cell resulting from progression of the disease which induces a mechanical distortion of the afferent and efferent fibers of the ANS. Ischemia and myocardial necrosis are followed by electrical re-modeling due to local nerve growth and degeneration at the level of the myocardial cell.[17,18] This results in the sympathovagal imbalance in the heart.

Thus apart from treating, the disease per se efforts have to be made at improving the autonomic balance of patients. Improvement in HRV can be achieved by introducing regular exercise and practise of yoga as a form of treatment of CAD.[19,20]

This study has the following limitation - short-term recording of HRV was used rather than ambulatory 24 h recording. However, it has been reported that frequency-domain analyses computed from 2- to 15-min segments were not meaningfully different from those calculated for 24 h, and they remained predictive of mortality.[21]

The second limitation of the study was selecting a sample that fulfilled the proposed inclusion criteria and avoiding other factors that influenced the HRV, thus the small sample size.

CONCLUSION

In this study, the patients with CAD showed increased sympathetic activity and reduced parasympathetic activity. This alteration in the balance between the branches of ANS puts them at a greater risk of adverse events such as arrhythmias and even sudden death. An attempt should be made at incorporating methods such as regular practice of yoga for the improvement of HRV as a modality of the treatment for these patients.

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