RESEARCH ARTICLE

ASSESSMENT OF AUTONOMIC FUNCTION WITH HEART RATE TURBULENCE AND HEART RATE VARIABILITY IN YOUNG OBESE PATIENTS

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ABSTRACT

Background: Sudden cardiac death (SCD) is a main cause of cardiovascular mortality in developed countries. Obesity-related impairment of the cardiovascular system may be exist even at the young age, and progress asymptotical for decades before clinical manifestations present in. Death may be sudden in obese individuals with or with- out arrhythmias Heart rate turbulence (HRT) and Heart rate variability (HRV) both of which reflects autonomic dysfunction is a proven non-invasive electrocardiographic predictor of cardiac death.

Aims & Objectives: To evaluate autonomic function with Heart rate turbulence (HRT) and Heart rate variability (HRV) in young obese patients without comorbidities.

Materials and Methods: 60 young patients with age ≤35 of body mass index (BMI) ≥30 (average 34.12 ± 2.59) and 40 young healthy patients with ≤35 of BMI <25 (23.25 ± 1.14) matched age and sex were divided in two groups (group 1: obese patients and group 2: Non-obese patients respectively). 24 hours ambulatory holter ECG recordings were obtained from all patients. Turbulence onset (TO), Turbulence slope (TS), Time domain HRV (SDNN, mean RR, RMSSD, sNN50 were analysed and compared between two groups.

Results: RMSSD (ms) and Total sNN50 was decreased in obese patients compared to non- obese patients (32.57 ± 7.40 vs 40.15 ± 6.80; p: 0.003 and 8616 ± 5300 vs 10920 ± 6700; p<0,001 respectively) and SDNN (ms) was decreased in obese patients compared those with no-obese. (122.79±23.19 vs 164.52±15.48 p<0,001 respectively). TS and TO was different between groups (8.85 ± 6.67 vs. 15.96 ± 12.37; p < 0,001 and 0.45 ± 1.62 vs -0.22 ± 0.32 respectively).

Conclusion: Autonomic dysfunction in young obese patients without comorbidities was impaired. These patients may be under risk of adverse cardiovascular outcome including fatal cardiac arrhythmias.

Key Words: Obesity; Autonomic Dysfunction; Arrhythmias; Young

Introduction

Sudden cardiac death (SCD) is a main cause of cardiovascular mortality in developed countries.[1] Obesity-related impairment of the cardiovascular system may be exist even at the young age, and progress asymptomatic for decades before clinical manifestations present in.[2] Death may be sudden in obese individuals with or with- out arrhythmias.[3] Previous studies have revealed that obese individuals are more likely to malignant arrhythmias than non-obese subjects. Therefore, obesity is a strong predictor of sudden death.[4] Studies proposed that obesity is related with cardiac autonomic dysfunction.[5] Decreased vagal function and increased sympathetic function both of which are risk factors predicting mortality was found in both healthy adults and adults with exit cardiovascular disease.[6-11] Heart rate turbulence, (HRT) and Heart rate variability (HRV) is a comprehensive analysis of cardiac autonomic reflexes.[12]

Our goal is to whether there is deterioration in autonomic function using combination of HRT and HRV in young obese patients without comorbidities.

Materials and Methods

Patients Selection: We selected 60 young obese patients with ≤35 age of BMI≥30 (mean age, 31.63 ± 2.8 years; and mean BMI: 34.12 ± 2.59) and 40 young healthy non-obese subjects with ≤35 age of BMI ≤25 (mean age, 31.85 ± 2.6 years; mean BMI: 23.25 ± 1.14) well balanced for gender, age. A detailed history and evaluation of patients was performed. The exclusion criteria were as follows: smoking habits, diabetes mellitus, hypertension, use of antihypertensive drugs, congestive heart failure, significant valvular heart disease, obstructive sleep apnea, pacemaker implantation, atrial flutter or fibrillation, frequent ventricular pre-excitation and atrio-ventricular conduction abnormalities, renal failure, previous myocardial infarction, or cerebrovascular accident. This study was conducted in accordance with the Declaration of Helsinki and was approved by our local ethics committee. Informed consent for the policy

was obtained from each patient.

Heart Rate Turbulence: Turbulence onset (TO) was defined as the difference between the mean of the first two sinus RR intervals after a Ventricular premature beat (VPB) and the last two sinus RR intervals before the VPB divided by the mean value of the last two sinus RR intervals before the VPB. The value of TO is expressed as a percentage. Positive values of TO (> 0%) indicate sinus rhythm deceleration after VPB, and negative values (< 0%) indicate acceleration. The optimal is TO < 0%. Turbulence slope (TS) is a measurement of the following heart rate deceleration. TS is the maximum positive slope of a regression line assessed over any sequence of five subsequent sinus rhythm RR intervals within the first 20 sinus rhythm intervals after VPB. The value of TS is expressed in milliseconds per RR interval. The normal value is over 2.5 ms/RR

Heart Rate Variability: Twenty-four hours Holter recordings taken from the subjects were downloaded onto a computer and analyzed with a Holter program (Reynolds Medical Pathfinder Software, Version V8.255, Hedford, England). All patients were in sinus rhythm throughout the recording period. All records were also examined visually and removed artifacts. All of the recordings had at least 22 hours of data. All of The HRV parameters were calculated by a computer and used in this study were chosen in time domains according to the guidelines of the European Society of Cardiology and North American Society of Pacemaker and Electrophysiology. HRV parameters were included as; standard deviations of all NN(normal-to-normal) intervals (SDNN), the number of interval differences of successive NN intervals greater than 50 ms (sNN50) and the square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD)

Statistical Analysis: The statistical analyses were performed using software (SPSS 18.0). Parametric values were given as mean ± standard deviation, and non-parametric values were given as a percentage. To compare parametric continuous variables, Student's t-test or analysis of variance was used; to compare nonparametric continuous variables, the Mann–Whitney U-test or the Kruskall–Wallis test was used. Categorical data were compared by Chi-square distribution. Two-tailed P-values of less than 0.05 were considered to indicate statistical significance.

Results

Age of patients was not difference between groups (31.63 ± 2.8 vs 31.85 ± 2.6 respectively). BMI of patients was different in two groups (34.12 ± 2.59 vs 23.25 ± 1.14). There was no differences in gender between two groups. Women compromised of 53% and 45% of obese and non-obese groups respectively. (p>0.05) HRT parameters in two groups were shown in table 1. There were no differences in Mean RR (ms). RMSSD (ms) and total sNN50 was decreased in obese patients compared to non- obese patients (32.57 ± 7.40 vs 40.15 ± 6.80 p: 0.003 and 8616 ± 5300 vs 10920 ± 6700 p<0.001 respectively) and SDNN (ms) was decreased in obese patients compared those with no-obese (122.79 ± 23.19 vs 164.52 ± 15.48 p<0.001 respectively). Parameters of HRT were shown in table 2. TS and TO was different between groups (8.85 ± 6.67 vs. 15.96 ± 12.37 p<0.001 and 0.45 ± 1.62 vs -0.22 ± 0.32 respectively). Percentage of abnormal Slope (figure 1) and Onset (figure 2) were higher in obese patients compared to non-obese patients.

Table-1: Heart rate variability (HRV) parameters of patients

	Obese	Non-obese	p value
Mean RR (ms)	774 ± 65	748 ± 88	>0.05
SDNN (ms)	122.79 ± 23.19	164.52 ± 15.48	<0.001
RMSSD (ms)	32.57 ± 7.40	40.15 ± 6.80	0.003
Total sNN50	8616 ± 5300	10920 ± 6700	0.001

Table-2: Parameters of heart rate turbulence (HRT)

	Obese	Non-obese	p
Total slope	8.85 ± 6.67	15.96 ± 12.37	<0.001
Total onset	0.45 ± 1.62	-0.22 ± 0.32	<0.001
Abnormal slope %	38.3	10.0	0.01
Abnormal onset %	61.7	15.0	0.01

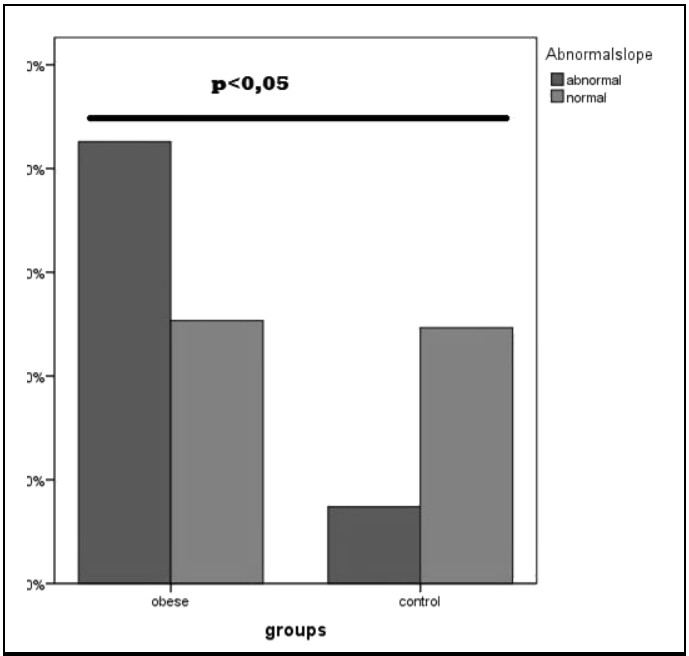

Figure-1: Percentage of abnormal slope in two groups

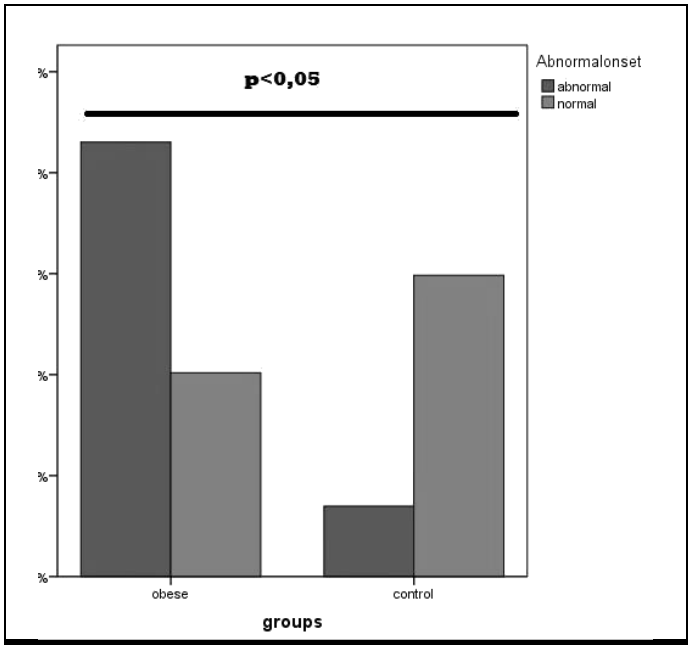

Figure-2: Percentage of abnormal onset in two groups

Discussion

In present study, we demonstrated that HRV was decreased in patients' young obese patients without comorbidities compared to those without obese. SDNN which reflects sympathetic and parasympathetic balance was decreased in obese patients Also, RMSD and SNN50 both of which are associated with parasympathetic modulation was decreased in obese patients. These findings of HRV suggest that balance between sympathetic and parasympathetic system was impaired and parasympathetic activation was decreased in obese patients Also, we showed that TS and TO and percentage of abnormal slope and onset were different between groups, and it was deteriorated in favour of obese patients without comorbidities. These parameters of HRT which reflects the presence of intact autonomic system was deteriorated in obese patients without comorbidities compared to non-obese patients.

The obesity epidemic is having a negative impact by increasing the risk of developing insulin resistance, type II diabetes, hypertension, dyslipidaemia, sleep apnoea syndrome, cardiovascular disease[13,14], sympathetic nervous system alterations[15,16], musculoskeletal complications, and certain forms of cancer[17]. Obesity and adipose tissue itself have direct and detrimental effects on cardiovascular function and structure through several mechanisms, including metabolic factors, inflammation, oxidative stress, endothelial dysfunction and sympathetic activation.[18] Also, there are significant pathologic findings in the conduction system in the sudden death of obese young people.[19] Studies suggest that obesity is associated with cardiac autonomic dysfunction.[5] Death may be sudden in obese individuals with or with- out arrhythmias.[3] Adachi et al suggest that modest, short-term weight gain is associated with increased cardiac sympathetic activity not only during wakefulness but also during sleep, which is reversible by weight loss in healthy individuals.[20]

An imbalance in autonomic nervous system function is a marker for increased cardiovascular risk and is associated with metabolic abnormalities including obesity, prediabetes, and diabetes.[21] Decreased vagal function and increased sympathetic function both of which are risk factors predicting mortality was found in both healthy adults and adults with exit cardiovascular disease.[6-11]

Heart rate variability (HRV) is widely used as a non-invasive tool that shows the balance of the cardiovascular system controlled by the sympathetic and parasympathetic divisions of the ANS.[22] It also can be used as a method for quantitative assessment of the ANS analysis because primary neural control of the heart is maintained by the ANS.[23] Several studies have demonstrated that reduced heart rate variability (HRV) in obese subjects, a strong indicator for autonomic disturbances that may be involved in the mechanism promoting arrhythmias and sudden death in obese subjects.[21,24] Kleiger et. al showed that decreased HR variability associated with mortality due to increased sympathetic or decreased vagal tone, which may lead to ventricular fibrillation.[25] Bigger et. al found that cardiac mortality after MI is strongly associated with decreased HRV.[26] Our finding was consisted with previous studies. In present study, we showed that SDNN which reflects sympathetic and parasympathetic balance were impaired in young obese patients without comorbidities. Also, RMSS and PN50 that indicator of parasympathetic modulation was impaired in young obese patients. These findings of HRV suggest that balance between sympathetic and parasympathetic system was impaired, and parasympathetic activation was decreased in obese patients

Heart rate turbulence (HRT) a comprehensive evaluation of cardiac autonomic reflexes.[12] HRT, which reflects a response of heart rate to a premature ventricular beat, is a new, non-invasive electrocardiographic predictor of cardiac death.[1,12,27] According to the European Society of Cardiology, HRT is an indicator of vagal activity and an

independent predictor of total mortality after myocardial infarction.[28] The assessment of HRT is an inexpensive and easy method and can be performed with a routine ambulatory 24-hour ECG recording.[29] TO and TS both of which are parameters of HRT are an indicator of the balance system between sympathetic and parasympathetic system. HRT needs an intact relationship of both, vagal and sympathetic systems. Absence of normal HRT can be resulted from changes in one of the systems.[30] The combination of abnormal TO and TS was also the strongest risk stratifies in a post infarction study (Autonomic Tone and Reflexes After Myocardial Infarction [ATRAMI]).[12] Cygankiewicz et al showed that usefulness of HRT parameters for predicting cardiac death in patients undergoing CABG.[31] HRT variables (especially HRT onset) were significantly decreased in Mitral valve prolapses(MVP) patients which may be associated with sudden death.[32] There are no sufficient data about HRT and obesity. Avşar et al. showed that HRT parameters seem to be normal in obese patients without comorbidities.[33] Erdem et al. showed that some HRV scores of ethnic Turkish Metabolic syndrome (MetS) patients are worse than the scores of ethnic Japan MetS patients. They suggested that these differences were related to the central obesity.[34] In our study, we showed that TS and TO was impaired in obese young patients without comorbidities. These findings reflect that balance system between sympathetic and parasympathetic system was impaired. Also, HRT which is an indicator of vagal system is impaired in the young obese patients without comorbidities, reflecting with drawing of parasympathetic system.

In a result, our study showed that autonomic function in young obese patients without comorbidities using combination of HRT and HRV were impaired. Impaired autonomic function is associated with poor cardiovascular outcome. These patients should be followed closed for poor cardiovascular outcome including fetal cardiac arrhythmias.

Conclusion

Autonomic dysfunction in young obese patients without comorbidities was impaired. These patients may be under risk of adverse cardiovascular outcome including fetal cardiac arrhythmias.

LIMITATION

The main limitation of our study seems to be the small sample size. Because the small sample size results in low statistical power for equivalency testing, negative results may be simply due to chance. We could not asses that whether these patients suffered with SCD in the future so long-term follow-up and comprehensive prospective studies are needed to determine the predictive value of HRT and HRV in this population.

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