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Cardiac Autonomic Function Evaluated by the Heart Rate Turbulence Method was not Changed in Obese Patients without Co-morbidities

Obese subjects are more prone to sudden deaths and arrhythmias than non-obese subjects. Heart rate turbulence (HRT) impairment reflects cardiac autonomic dysfunction, in particular impaired baroreflex sensitivity and reduced parasympathetic activity. Our aim was to evaluate the cardiac autonomic function in obesity by the HRT method. Ninety obese subjects and 112 healthy subjects were included in the study. Twenty-four hours ambulatory electrocardiograms were recorded and Holter recordings were analyzed. HRT parameters, turbulence onset (TO) and turbulence slope (TS), were calculated with HRT View Version 0.60-0.1 software program. HRT were calculated in 43 obese and 43 control subjects who had at least one ventricular premature beat in their Holter recordings. We excluded 47 obese patients and 69 control subjects who showed no ventricular premature beats in their Holter recordings from the statistical analysis. There were no significant differences in TO and TS between obese and control subjects (TO obese: -1.6±2.2%, TO control: -2.1±2.6%, p>0.05; TS obese: 8.2±5.2, TS control: 10.1±6.7, p>0.05, respectively). HRT parameters seem to be normal in obese patients without co-morbidities.

Key Words : *Obesity; Heart Rate; Autonomic Nervous System*

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INTRODUCTION

Obesity, a condition characterized by hyperinsulinemia and insulin resistance, causes a whole spectrum of subsequent health problems (1, 2). Obese subjects suffer from an increased mortality and morbidity risk due to cardiovascular complications (3).

The cause of this increased cardiac risk may be the alternations in autonomic function. The relationship between sympathetic nervous system activity and obesity has long been studied. Human studies examining adrenergic activity in obesity have given conflicting results (4-6). However, a decrease in parasympathetic activity has consistently been reported in obesity (1).

Intact autonomic cardiac control appears to be an important protective factor in the pathophysiology of malignant arrhythmias and sudden cardiac death (7). Previous studies have shown that obese subjects are more prone to malignant arrhythmias than non-obese subjects. Therefore, obesity is a strong predictor of sudden death (3). Several investigators have reported 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 (8, 9).

Heart rate turbulence (HRT) was recently introduced as an indicator for the physiologic changes in the sinus cycle that follow the occurrence of ventricular premature beat (VPB) (10). HRT impairment reflects cardiac autonomic dysfunction, in particular, impaired baroreflex sensitivity (BRS) and reduced parasympathetic activity (11). HRT can be used as a non-invasive measure of cardiac autonomic dysfunction (12). According to the European Society of Cardiology, HRT is an indicator of vagal activity and an independent predictor of total mortality after myocardial infarction (13). It has been shown that there is a relationship between HRT parameters and cardiovascular outcomes.

In obesity, autonomic control on cardiac function involvement is controversial. Therefore, the aim of the present study was to evaluate the cardiac autonomic function in obesity by the HRT method.

MATERIALS AND METHODS

Study population

Ninety consecutive obese patients who applied to the Internal Medicine and Cardiology Departments of Afyon Kocatepe University, School of Medicine Hospital due to various nonspecific complaints and obesity were included in this study. The subjects with unstable angina, myocardial infarction, heart failure, hypertension, diabetes mellitus, val-

vular heart disease, non-sinus rhythm, hyperthyroidism, left ventricular hypertrophy, electrolyte disturbances or other systemic disorders (e.g. chronic renal failure and hepatic failure) were excluded as well as those who were smokers or on cardioactive drug medication (especially beta blockers and/or antiarrhythmic drugs). The obesity was defined as a body mass index (BMI) ≥ 30 kg/m^2 (BMI was calculated as the weight in kilograms divided by the square of the height in meters) (14). Approximately in half of patients, BMI was between 30 and 34.9 kg/m^2. In the remaining patients, BMI was between 35 and 39.9 kg/m^2. The control group consisted of 112 age-matched healthy volunteers. In both groups, anamnesis and physical examination, routine biochemical and hematological tests including fasting blood glucose, blood urea nitrogen, lipids, serum electrolytes, thyroid hormones and hemoglobin, resting 12-lead electrocardiogram (ECG), transthoracic echocardiography, and treadmill exercise test were performed. According to the ATP III criteria of metabolic syndrome, there was no subject with metabolic syndrome in obese patients.

Signed written consent was obtained from all subjects before their participation in the study, which was approved by the local ethics committee of our institution.

HRT analyses

All participants (90 obese and 112 control subjects) underwent 24-hr Holter ECG. Holter recordings were analyzed with Reynolds Medical Pathfinder Software Version V8.255 (Reynolds Medical, Hedford, England). Firstly, while determining HRT, abnormal beats and areas of artifact that were accepted as VPB by computer were excluded, if they are not manually identified so. In order to calculate HRT, there must be at least one proper VPB in the entire Holter recording. Measurements of HRT were done by the original method (10). Turbulence onset (TO), which is a measure of the early sinus acceleration after a VPB, is expressed as percentage and is calculated with the following formula: $[(RR_1+RR_2)-(RR_{-2}+RR_{-1})]/(RR_{-2}+RR_{-1})\times 100$, where RR_1 and RR_2 are the first and second sinus RR intervals after the VPB, respectively, and RR_{-1} and RR_{-2} are the first and the second sinus RR intervals preceding the VPB, respectively. Turbulence slope (TS), which is a measure of the late sinus deceleration after a VPB, is obtained as the maximal positive slope among all slopes of a series of regression lines obtained from all sequences of 5 consecutive RR intervals included between the first and the 20th RR interval following the VPB, and expressed as ms/RR. TO was calculated for all VPB's separately and then averaged, whereas TS was calculated based on an averaged local tachogram.

Statistical analysis

All the values are expressed as means $\pm$ SD. Statistical analyses were performed with SPSS for Windows version 10.0 (SPSS Inc. Chicago, IL. U.S.A.). Differences between groups were analyzed by the Student's unpaired t test and chi-square test, as appropriate. A p value <0.05 was considered as statistically significant.

RESULTS

Since there were no VPB in Holter recordings of 47 obese patients and 69 control subjects, these subjects were excluded from the statistical analysis. As a result, HRT parameters were calculated in 43 obese patients (mean age 45.6 ± 10.2 yr, ranged from 27 to 66 yr, 23 women) and in 43 control subjects (mean age 44.3 ± 10.6 yr, ranged from 22 to 63 yr, 22 women). The demographic and clinical characteristics of the two study groups are shown in Table 1. The obese patient group was homogeneous.

HRT onset and slope did not differ significantly between obese subjects and controls (TO obese: $-1.6\pm2.2\%$, TO control: $-2.1\pm2.6\%$, $p>0.05$; TS obese: 8.2 ± 5.2, TS control: 10.1 ± 6.7, $p>0.05$, respectively, Fig. 1).

DISCUSSION

Obesity-related cardiovascular complications have been attributed to chronic stimulation of sympathetic activity, imposing a functional overload on the heart and the vasculature (15). In subjects with uncomplicated obesity, chronic hyperinsulinemia is associated with persistent baroreflex down-regulation and postprandial sympathetic dominance. It has been shown that these changes are reversed by weight loss (9).

The heart is richly innervated by afferent and efferent vagal and sympathetic fibers and is, thus, susceptible to autonomic influences (16). So, the changes in efferent autonomic traffic to the heart play a critical role in the genesis and outcome of cardiac arrhythmias. Increased sympathetic and decreased

Table 1. The demographic and clinical characteristics of the two study groups

	Obese patients (n=43)	Control subjects (n=43)	p value
Age (yr)	45.6 ± 10.2	44.3 ± 10.6	>0.05
Gender (Male/Female)	20/23	21/22	>0.05
Body mass index (kg/m^2)	35.6 ± 5.2	23.4 ± 2.2	<0.001
Waist circumference (cm)	105 ± 11	73.1 ± 3.2	<0.001
Heart rate (beats/min)	74 ± 9	76 ± 10	>0.05
Systolic blood pressure (mmHg)	121 ± 17	118 ± 21	>0.05
Total cholesterol (mg/dL)	197 ± 39	191 ± 35	>0.05
LDL-cholesterol (mg/dL)	119 ± 32	115 ± 30	>0.05
Triglyceride (mg/dL)	153 ± 79	145 ± 68	>0.05

LDL, low-density lipoprotein. Values are means $\pm$ SD.

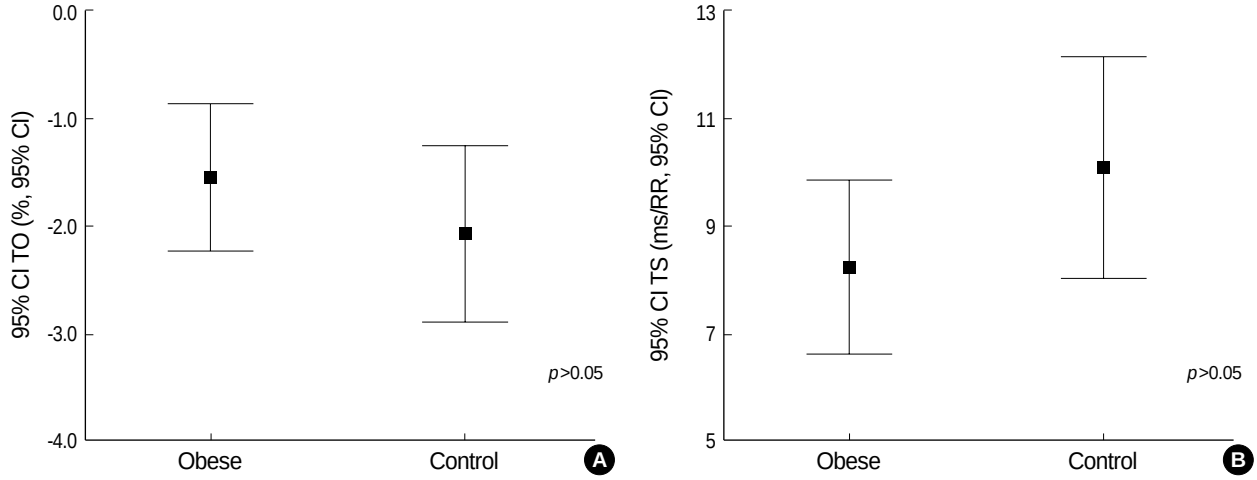

Fig. 1. Turbulence Onset (TO, A) and Turbulence Slope (TS, B) values of the two study groups. CI, confidence interval.

vagal tone can interact with all of the electrophysiological mechanisms underlying arrhythmogenesis. The fact that changes in efferent autonomic traffic are largely under baroreceptor control explains why baroreceptor function is correlated with cardiac arrhythmias (17). HRT, BRS, and HRV provide different information about cardiac autonomic function, and they are predictors for mortality in heart diseases (18). Moreover, the moderate correlation between BRS and HRV (r=0.63) suggests that the two measures explore different functions of autonomic control (19).

In obese subjects, autonomic function has been investigated using HRV. The autonomic dysfunction has been shown in a few studies in obesity (9, 20). Also, it has been shown that changes of 10% body weight influences HRV. Some authors showed that a 10% weight gain significantly decreased HRV, which was attributable to decreased parasympathetic activity (20). Arone et al. showed that a 10% weight loss increased parasympathetic activity and decreased sympathetic activity in both non-obese and obese subjects (21). However, autonomic dysfunction has not been shown in other studies (22, 23).

HRT is highly correlated with spontaneous BRS, and it may be used instead of BRS (24). It is proven that HRT also predicts mortality and sudden cardiac death in various cardiac diseases, such as after myocardial infarction (10), after coronary artery by-pass grafting surgery (18), and in chronic heart failure (25). In addition, HRT predicts alterations of autonomic cardiac function in diabetes mellitus (26) and hyperthyroidism (27). However, the implication of HRT has not been studied in obesity.

In our study, we found that HRT, which may be used instead of BRS, remains normal in obese subjects. This finding was not similar with that of Hofmann et al. who found that BMI and waist/hip ratio were inversely correlated with sympathetic activity and BRS was strongly related to the degree of obesity (1). In addition, some researchers did not find any deterioration in cardiac autonomic function in obese subjects by using HRV (22, 23). In the present study, cardiac autonomic function that was determined by HRT was also found normal. The negative results here may be due to the fact that the patient population was different in the present study. The difference was that the patient population had no co-morbidities. Besides, the fact that those HRT indices may indicate a different aspect of the autonomic nervous system activity compared with HRV or BRS. Ortak et al. have shown that in the same patient group after myocardial infarction the indices of HRV were increased but HRT parameters were not changed (28).

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. However, it should be taken into account that establishing an obesity group without co-morbidities (e.g. diabetes mellitus, hypertension, cardiovascular and renal disorders) is difficult. Secondly, we did not make subgroup analysis in our study according to the obesity grade because the classification of patients according to BMI would decrease the sample size in subgroups. In this situation, the statistical power of these subgroups would decrease, too.

In conclusion, although obesity is associated with excess cardiovascular morbidity and mortality, in our study, HRT parameters, which determine the risk of sudden death, did not alter in obese patients without co-morbidities. Therefore, weight gain without co-morbidities may not affect cardiac autonomic function, and the main reason of cardiac autonomic dysfunction in obesity may be the concomitant disorders. Simple obesity without metabolic syndrome may not have significant effects on the autonomic function. Of course, we need further comprehensive studies in obese patients in this respect.

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