EFFECT OF OBESITY ON ELECTROCARDIOGRAPHIC PARAMETERS OF VENTRICULAR REPOLARIZATION IN HEALTHY ADULTS

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ABSTRACT

BACKGROUND
Obesity affects the different organ systems of our body and has been recognized as a key risk factor for many diseases Most of the abnormalities of cardiovascular system, developing as a result of obesity, reflect alterations in cardiac morphology or conduction defects. These abnormalities are reflected in ECG as prolongation of various intervals. The aim of the study was to find the association between obesity and these ECG markers.

MATERIALS AND METHODS
96 healthy males of age group 20-39 years were included in the study. Relevant medical history and anthropometric variables were taken. Subjects were divided into normal, overweight and obese groups based on BMI. The body fat percentages were calculated after taking skinfold measurement. ECG recording was done for each subject and different parameters were calculated.

RESULTS
QT and QTc intervals were found to be significantly higher in obese subjects compared to normal as well as overweight subjects. Significant, positive correlation was found between QT, QTc, Tpe and parameters of obesity i.e. BMI, WHR and body fat %.

CONCLUSION
Obesity leads to lengthening of ventricular action potential as shown by increased QT and QTc interval.

KEYWORDS
Obesity, B.M.I., Body Fat %, ECG, QT Interval, QTc Interval.

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BACKGROUND

Obesity is a condition in which there is an excess of body fat. It is defined by WHO as abnormal or excessive fat accumulation that presents a risk to health.[1] It affects the different systems of our body and has been recognized as a key risk factor for many diseases.

BMI (body mass index) is the most commonly used variable to classify individuals as overweight or obese because of its feasibility and ease of interpretation. Since decades, it has been used to study the effect of obesity on various organ systems.[2,3] But as the definition suggests, obesity is related to excessive body fat percentage rather than one's body weight. A person may be overweight without being obese. Extra weight may be due to better bone and muscular development, both heavier than adipose tissue. In early studies, besides BMI, another parameter Waist-to-Hip Ratio (WHR) is often used for body fat distribution. There is doubt whether WHR, which is partly dependent on pelvic skeletal structure and muscle distribution, is a valid anthropometric measure for the assessment of body composition.[4] Due to this reason, an alternative method to determine body fat percentage might also be used. It includes measurement of skinfold and girth anthropometrically.[5] Skinfold ratios have been widely used for the assessment of fat distribution and correlate well with several factors of cardiovascular disease.[6,7]

Most of the abnormalities of cardiovascular system, developing as a result of obesity, reflect alterations in cardiac morphology or conduction defects. The ECG abnormalities seen in obese as compared to non-obese individuals include shift of P-wave, lengthened wave durations, axis deviations and low voltage complexes.[8] Master et al.[9] reported that 86% of 97 obese patients had left axis deviation. Proger et al.[10] noted that 71% of 55 patients with uncomplicated obesity had a left axis deviation. In these early studies, the definition of both obesity and left axis deviation was arbitrary and imprecise.

Electrocardiographic markers that are commonly used to study sympathetic activation are heart rate (HR) and HR variability.[11] Some of recent experimental studies showed that the sympathetic overdrive is also reflected in other changes on the standard electrocardiogram.[12] These

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changes include alterations in conduction times and ventricular repolarization. Prolongation of the QT interval on the ECG represents delayed repolarization of the ventricular myocardium. Myocardial repolarization has been assessed using various methods, including QT dispersion (QTd) and corrected QT dispersion (cQTd).[13] Nowadays interest has grown in new electrocardiographic parameters of ventricular repolarization; the Tpeak-Tend (Tpe) interval, its dispersion (Tpe-d), and the relationship between Tpe interval and QT interval (Tpe/QT ratio).[14,15] These parameters can be used as an index of dispersion of repolarization.

In this study, the various electrocardiographic parameters associated with obesity were examined in the overweight and obese persons. These parameters were also compared with that of a normal population. The objective of the study was to find the association between obesity and these ECG markers.

MATERIALS AND METHODS

Design of the study was cross sectional and total 96 male subjects aged between 20 to 39 years participated voluntarily in the study. The study protocol was approved by the Institutional Ethical Committee. Written informed consent was taken from each subject before entering in the study and purpose of the study was explained to the subjects. The subjects were informed about the risks and benefits of the procedure.

Subjects were divided into normal, overweight and obese groups based on BMI; normal with BMI less than 25, overweight: 25-30 and obese: more than 30 kg/m^2.

Non-compliant subjects, smoker and subjects with history suggestive of disorders of respiratory system, cardiovascular disease, endocrinal e.g. thyroid, diabetes mellitus etc were excluded from study.

Exclusion of metabolic syndrome was done according to NCEP – ATPIII criteria.[16] which require the presence of three or more of the following five factors- a) abdominal obesity: waist circumference greater than 88 cm for women and greater than 102 cm for men; b) plasma level of triglycerides ≥ 150 mg/dl; c) plasma level of HDLc lower than 40 mg/dl for men and 50 mg/dl for women; d) systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg; e) fasting blood glucose ≥ 110 mg/dl.

Baseline Characteristics of Subjects

Patients' general information such as age, height, weight waist circumference, hip circumference were measured.

Height and weight of the subjects were measured using a standardized height and weight machine known as Samso height scale and GF electronic weighing scale respectively. For this, the subjects were lightly clothed but without shoes. Standing height was measured to the nearest 0.5 cm. The subject stood against a standard meter scale, ears and the infra-orbital margins lay in one horizontal plane. Body weight was recorded in kilograms on an empty bladder and before lunch on a standardized weighing scale. The weight measurement was recorded to the nearest 0.1 kg.

Waist circumference & Hip circumference.[17]- Waist circumference measurement was done with minimal clothing with feet 25–30 cm apart with a measuring tape at the level of umbilicus between the inferior margin of the last rib and the iliac crest without compression of the skin with nearest to 0.5 cm. Hip circumference measurement was done with minimal adequate clothing by a measuring tape at the most protuberant area of buttocks without compressing the skin.

After taking body circumference and height and body weight, the following parameters were calculated: -

1. Waist hip ratio- It is the measure of central pattern of fat distribution.

WHR= waist circumference/hip circumference

2. Body mass index (BMI) = Weight (kg)/ $Height^2$ (m^2)

Skinfolds were measured with a Harpenden caliper (Holtain, UK) to the nearest 0.1 mm according to the recommendations of the International Biological Programme.[18,19] and with the same instruments throughout the study. The measurements were taken at four anatomical sites - biceps, triceps, subscapular, supra-iliac region. The thickness of the double layer of skin and subcutaneous tissue was read directly from caliper dial and recorded in millimeters (mm) within 2-5 seconds after applying the full force of caliper. All skinfolds were taken on the right side of the body. Body density in gm/cc was derived from the sum of these four skin fold thickness scores using regression equations of Durnin & Womersley.[20] as:

Body Density = c- m x log (sum of skin fold thickness measurements at 4 sites in mm)

Where c and m values are two constants (different for age and gender).

Body fat percentages were determined according to Siri equation.[21]:

% Body fat content = ((4.95/ Body density) - 4.50) x 100.

Electrocardiographic Recording

The electrocardiographic recording was done using Magic RSA -12 ECG machine by Maestros Medline system Ltd. Before recording leads, ECG machine was tested and adjusted as 1 mV should be equal to 10 small square or 1 cm. The speed of ECG paper was 25 mm/sec. A resting ECG was recorded in lying posture after duly assuring them the noninvasive nature of the procedure.

All ECG data were scanned and transferred to personal computer. After doing 400% magnification, the following parameters were calculated with Adobe Photoshop software:

QT, QTc, QTd, QT apex dispersion (QTapex-d), Tpe, Tpe-d, and Tpe/QT ratio.

Subjects with U wave on their ECG were excluded from the study. QT interval length was measured from lead II from beginning of QRS complex to end of T wave. The QTc interval was obtained using Bazett's formula.[22,23] QT dispersion was determined as the difference between the maximum and minimum QT intervals.[24] The Tpe interval was measured in all precordial leads and obtained from the difference between QT interval and QT peak interval, measured from the beginning of the QRS to the apex of the

T wave. The Tpe-d was defined as the difference between the maximum and the minimum Tpe interval in the precordial leads.[25] Tp-e/QT ratio was calculated from these measurements. The Tpe/QT ratio is the ratio of the interval from the peak to the end of the T wave divided by the interval from the onset of the Q wave to the end of the T wave and it was measured using V_5.[26]

Statistical Analysis- Statistical analysis was performed using SPSS 17.0. The difference between the groups was analysed using a one-way ANOVA for each variable. Tukey's post hoc test was done to evaluate from which difference the significance originated. The Pearson correlation test was used for the correlation analyses. Significance was set at p <0.05. Graphs and charts were made in Excel 2007.

RESULTS
The present study was conducted to study the effect of obesity on cardiovascular physiological parameters in young adults. Baseline anthropometric measurements (age, height, weight, waist circumference and hip circumference) of all the subjects were taken. Then BMI and WHR were calculated. The subjects were divided in 3 groups: normal, overweight and obese based on BMI. Body fat% was calculated by taking four sites skinfold thickness. These baseline parameters are shown in Table 1.

Variables	Normal Weight (n=34)	Overweight (n=30)	Obese (n=32)	p-value
Age (years)	28.81 ± 3.75	28.99 ± 2.78	30.12 ± 1.95	>0.05
B.M.I.(kg/m^2)	21.29 ± 2.27	27.86 ± 1.61*	34.17 ± 2.45†,‡	<0.01
WHR	0.80 ± 0.05	0.84 ± 0.04 *	0.98 ± 0.08 †,‡	<0.01
Body Fat %	12.88 ± 1.15	17.78 ± 1.27 *	22.59 ± 1.50 †,‡	<0.01

Table 1. Baseline Anthropometric Characteristics of the Study Population

All data are shown as mean ± SD, p - values were calculated by ANOVA.
*, †: p<0.05 vs. normal; ‡: p<0.05 vs. overweight.

Mean values of QT, QTc, QTd, QTapex-d, Tpe, Tpe-d, and Tpe/QT ratio in the normal weight, overweight and obese group are shown in Table 2. Obese group subjects showed significantly higher QT and QTc value compared to normal as well as overweight subjects (Fig. 1, Fig. 2). QTd, QTapex-d, Tpe, Tpe-d values were higher in obese group but not significantly increased (Table 2, Fig: 3). Tpe/QT ratio showed very narrow range and there was no meaningful difference between the groups.

Variables	Normal Weight (n=34)	Overweight (n=30)	Obese (n=32)	p-value
QT (ms)	338.24 ± 18.76	358.13 ± 26.25*	368.12 ± 24.65†	<0.01
QTc (ms)	374.83 ± 18.18	390.17 ± 18.98*	413.56 ± 31.35†,‡	<0.01
QTd (ms)	29.38 ± 10.60	31.75 ± 10.17	34.10 ± 12.44	>0.05
Tpe (ms)	86.47 ± 13.32	87.04 ± 17.01	90.27 ± 11.77	>0.05
Tpe/QT	0.21 ± 0.03	0.22 ± 0.02	0.22 ± 0.03	>0.05
Tpe-d	26.24 ± 13.16	24.45 ± 9.46	30.36 ± 12.56	>0.05
QTapex-d	23.86 ± 11.50	25.75 ± 11.39	30.27 ± 12.24	>0.05

Table 2 Electrocardiographic Parameters in the Three Groups

All data are shown as mean ± SD, p- values were calculated by ANOVA.
*, †: p<0.05 vs. normal; ‡: p<0.05 vs. overweight.

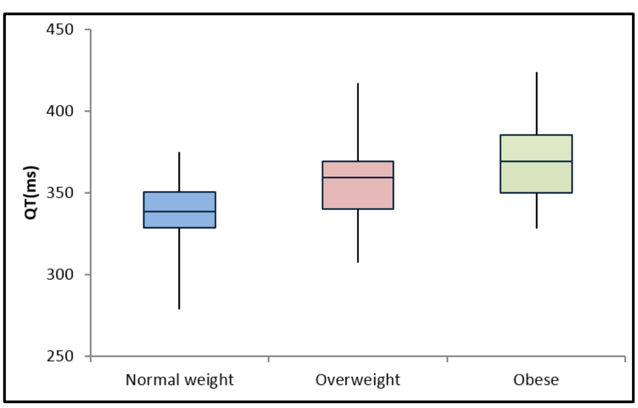

Figure 1. Boxplot Showing QT Interval in the Groups

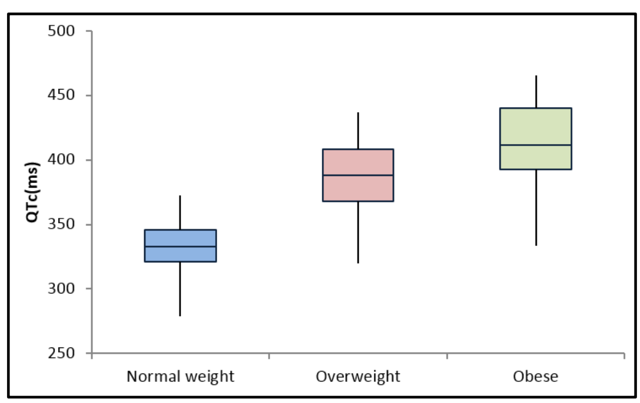

Figure 2. Corrected QT Interval in the Study Groups

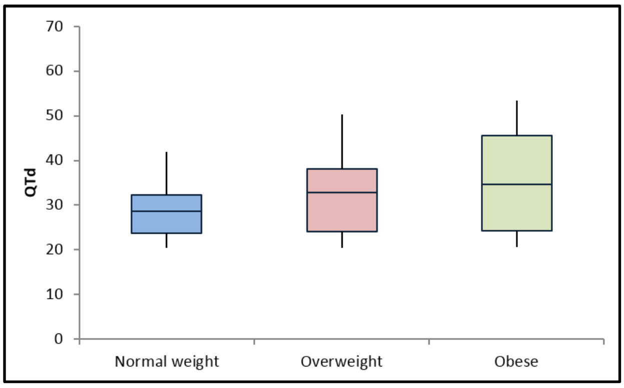

Figure 3. QT Distribution in the Groups

To study the effect of obesity on cardiac repolarization parameters, correlation analysis was done. Pearson correlation coefficients were computed to assess the relationship between the ECG variables and obesity associated measurements, including BMI, waist- hip ratio and body fat %. These results (Table 3, 4, 5) show that QT, QTc and Tpe shows positive significant correlation with all physical parameters i.e. BMI, WHR and body fat %. QTd, QTapex-d, Tpe-d, and Tpe/QT ratio also showed positive relation but not significant.

Variables	QT	QTc	QTd	Tpe	Tpe/QT	Tpe-d	QTapex-d
r	0.26	0.37	0.39	0.21	0.22	0.34	0.35
p value	<0.05	<0.05	>0.05	<0.05	>0.05	>0.05	>0.05

Table 3. Pearson correlation coefficients of various ECG parameters with BMI in the study population (n=96)

Variables	QT	QTc	QTd	Tpe	Tpe/QT	Tpe-d	QTapex-d
r	0.29	0.54	0.31	0.25	0.37	0.28	0.25
p value	<0.05	<0.05	>0.05	<0.05	>0.05	>0.05	>0.05

Table 4. Pearson correlation coefficients of various ECG parameters with Waist Hip Ratio (WHR) in the study population

Variables	QT	QTc	QTd	Tpe	Tpe/QT	Tpe-d	QTapex-d
r	0.38	0.56	0.41	0.28	0.27	0.38	0.31
p value	<0.05	<0.05	>0.05	<0.05	>0.05	>0.05	>0.05

Table 5. Pearson Correlation Coefficients of Various ECG Parameters with Body Fat % in the Study Population

DISCUSSION

Obesity is a complex condition and an independent risk factor for cardiovascular morbidity. Even in absence of comorbid conditions and underlying organic heart pathologies, obesity is able to provoke alterations in both the morphology and in the electrophysiology of myocardial cells. Obesity is closely associated with a wide variety of ECG changes. In obese subjects, compared to normal weight subjects, a significant lengthening of QT and QTc has been shown. QT dispersion is also lengthened in obese persons but not significantly. The QT interval reflects the total duration of ventricular myocardial depolarization and repolarization. Prolongation of QT on a standard 12-lead electrocardiogram is caused by lengthening of the action potential of ventricular myocytes. QT dispersion, instead, measures indirectly the heterogeneity of repolarization, caused by regional variations in the duration of the action potentials.

QT and QTc have been reported to be increased in obesity and appear influenced by autonomic tone. It seems that there is a relationship between free fatty acids, cardiac sympathetic nervous activity and repolarization abnormalities; the autonomic dysfunction with a sympatho-vagal imbalance is a potential mechanism underlying QT prolongation in obese subjects.[27]

Our study shows that QTd and QTd-apex present a tendency toward increase, comparing normal weight to overweight subjects, and overweight to obese subjects; though these differences don't reach statistical significance. In our study, none of the other repolarization parameters showed significant differences between the groups. TPe and TPe-d showed slightly higher duration in obese group when compared to overweight. It was seen that mean TPe/QT ratio coincided in the two groups. An additional finding of our study is significant positive correlation of QT, QTc and TPe with BMI, WHR and body fat percent.

These findings confirm previous studies of the ECG parameters in obesity. Frank et al[28] found a low but statistically significant relationship between percent overweight and QTc interval in obese patients. In addition, El-Gamal et al[29] found significant correlations between QTc intervals and both BMI and %BF in healthy obese people.

Waist hip ratio and body fat % were strongly associated with QTc than BMI. No significant associations of BMI, WHR or body fat% were observed with QTd, TPe/QT, TPe-d and QTapex-d.

Total body fat % and waist hip ratio, reflect body fat and to some extent body fat distribution also. BMI may not be valid measure to describe body composition because it does not distinguish between body fat and lean body mass. This indicates that different fat depots within the abdomen do not only differ in localization but also in function and that the visceral fat depot is most important with regard to sympathetic activation.

In earlier papers, total body fat was associated with different measurements of the autonomic nervous system, as was waist circumference.[30,31]

An increase in body fat significantly alters the autonomic functioning of body reflected in various ECG variables. Body fat was associated with measures of sympathetic activation in subjects with structurally normal hearts in the NEO study.[32]

The increased QT and QTc interval in our study can be explained by the slowed conduction in the cardiac muscle due to increased amount of fatty tissue in the cardiac musculature. According to Frank et al. as body weight increases, cardiac conduction of impulse is slowed and their QRS vector shifts towards the left. Finally, in line with our results, a recent paper observed an association of BMI with QTc, but not with Tpeak-end.[33] The increased waist-hip ratio of obese subjects also indicates towards their upper body obesity. This increased waist-hip ratio may be one of the causes for significantly increased QTc interval.[34]

CONCLUSION

In the study, the only parameters that changed in a statistically meaningful way between normal weight and overweight/obese subjects were represented by QT and QTc; therefore, it could be concluded that obesity leads to prolonged duration of ventricular action potential. Also, general body fat (BMI, total body fat percentage) and abdominal body fat (WHR) are significantly associated with QT, QTc, and TPe.

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