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A Comparative Study of QTC in Obese, Non-Obese Hypertensive and Obese Normotensive Males

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Abstract

Background: QTc (corrected QT interval) is an index of physiological variability of ventricular repolarization. Prolonged QTc has been reported in cardiac failure, arterial hypertension, ischaemic heart disease and in obesity.

Aims and Objectives: This study was aimed at evaluating the effect of hypertension and obesity on QTc. The objective of the study was to compare the QTc in obese, non-obese hypertensive and normotensive obese male subjects.

Method: We compared the QTc in obese-hypertensives (n=15), in nonobese hypertensives (n=15) and in obese-normotensives (n=15), comparable for age and sex. Blood pressure was measured in supine position by mercury sphygmomanometer. Body mass index (BMI), WC (waist circumference) and WHR (waist hip ratio) of all patients were calculated.

Results: QTc was longer in obese hypertensives and obese normotensives compared to nonobese hypertensives($p<0.00$). WC and WHR had positive correlation with QTc prolongation in obese hypertensives and obese normotensives.

Conclusion : This study indicates that obesity is an important predictor of QTc prolongation than blood pressure. Waist circumference and WHR which reflects abdominal obesity have greater association with QTc prolongation.

Keywords: *hypertension, QT interval, obesity, Bazett's formula*

Introduction

Electrocardiogram is a useful tool to detect cardiac changes with hypertension.[1] QTc is an index of physiological variability of ventricular repolarization and an increase of QTc is a possible risk factor for ventricular arrhythmias and sudden death.[2]

Hypertension is defined as persistent elevation in blood pressure ≥ 140/90 mmHg. The prevalence of hypertension in India is 23.10 % men and 26.60% women.[3] Prevalence of hypertension in South India is found to be 20% according to 2007 CURES study.[4] It is recognized as a common cardiovascular disease and a major risk factor for congestive heart failure, ischemic heart disease, chronic renal failure and stroke. cardiac damage is a common early complication of hypertension.[1]

Obesity has been reported as the cause of QT interval prolongation. QTc prolongation has also been associated with abnormalities of insulin and glucose metabolism with a preponderance to make age, hypertension, diabetes mellitus, hypercholesterolemia, fibrinogen and BMI. There was significant association between BMI and electrocardiographic values such as P wave and QTc dispersion which were increased.[5]

Prolonged QTc is an index of sympathetic over activity under several cardiac conditions and previous studies have shown that increased sympathetic activation is present in both obesity and hypertension particularly when two conditions coexist.[2]

This study was aimed at evaluating the effect of hypertension and obesity on QTc.

Objectives

To compare the QTc in obese, non-obese hypertensive and normotensive obese male subjects.

Materials and Method

This study was conducted in Sri Manakula Vinayagar medical college hospital Madagadipet, Puducherry. This was a hospital-based case control study. This study was approved by the Institutional Ethics committee, Sri Manakula Vinayagar medical college hospital.

The sample size was 45 subjects aged 35-55 years and they were divided into three groups

15 obese hypertensive male subjects of 35-55 years of age- Group 1

15 obese normotensive male subjects of 35-55years of age – Group2

15 non-obese hypertensive male subjects of 35-55years of age – Group3

Inclusion criteria

1. Male subjects 35 -55 years of age.

2. Obese Hypertensive subjects having blood pressure ≥140/90 mmHg (according to WHO criteria)

3. Non-obese Hypertensive subjects having blood pressure ≥140/90 mmHg (according to WHO criteria)

4.Obese normotensive subjects having blood pressure ≤120/80mmHg.

Exclusion criteria

H/o cardiovascular disease

H/o respiratory disease

H/o drug, Medications

H/o renal disease

H/o endocrine disease

1. Measurement of Blood pressure:

Blood pressure was measured by a mercury sphygmomanometer in supine position. Blood pressure was measured two times. The average of two readings was taken as correct systolic and diastolic blood pressure.[6]

The classification of blood pressure is as follows

Normal BP: <120/80 mmHg

Prehypertension: 120-139/ 80-89 mmHg

Stage I Hypertension: 140-159 / 90-99 mmHg

Stage II Hypertension: > 160/100 mmHg.

2. Body weight:

Body weight was measured while the subject minimally clothed and without shoes, standing steady on a weighing scale and it was recorded to the nearest 0.1kg.[7]

3. Height:

Height was measured to the nearest 0.1 cm while the subject was standing barefoot in erect position with a wall mounted stadiometer.[7]

4. Body mass index:

BMI was measured by weight in kilograms divided by square of height in meters (kg/m2).

(BMI in the range of 18.50 to 24.99 kg/m2 is considered to be normal.[7]

5. Waist circumference:

Waist circumference was measured in centimeters over light clothing at a point mid-way between the lower rib and iliac crest.[7]

6. Hip circumference:

Hip Circumference was measured in centimeters over light clothing at the widest girth of the hip. For waist and hip circumference two consecutive readings were made at each site on a horizontal plane without compression of the skin. The mean was taken as the final reading. [7]

7. Waist Hip Ratio: It was calculated by dividing waist circumference by hip circumference.[7]

8. Electrocardiography

ECG is the graphical record of electrical activity of heart obtained by placing electrodes on the surface of the body that records voltage differences generated by the heart. Using a standard 12 conventional ECG lead,

the difference in potential was recorded. QT interval was measured from the earliest onset of QRS complex to the terminal portion of the T wave where it meets the baseline. QT interval was measured by computerized measurements from limb lead II. RR interval from the preceding cardiac cycle was measured from the peaks of the R waves to correct the QT interval for heart rate (QTc). QT intervals was corrected with Bazzet's formula which was done by the computer. ($QTc=QT/\sqrt{RR}$).[2]

Based on European regulatory guidelines to stratify baseline QTc prolongation (ms) in men:

Normal QTc prolongation ≤ 430ms

Borderline QTc prolongation 431–450ms

Abnormal QTc prolongation ≥ 451ms.[8]

Statistical analysis

The data collected were entered and analyzed using software Statistical Package for the Social Science 16.0 (SPSS 16.0). All parameters were presented as mean ± standard deviation (mean ± SD). Comparison of parameters between various groups was done with student 't' test. Correlation analysis was done with Pearson's correlation method. A linear regression analysis was performed to evaluate the independent predictors of QTc. A p value of less than 0.05 was considered statistically significant.

Results

The results were presented as mean ± standard deviation in table 1. Table 1 summarizes the descriptive statistics of anthropometric measurements, ECG recordings and blood pressure among the three groups. The mean values of QTc were significantly increased in obese hypertensives in comparison with the obese normotensives and nonobese hypertensives ($p<0.05$).

Table 2, 3 and 4 shows the correlation of anthropometric indicators with QTc. WHR, WC and BMI were found to be positively correlated with QTc among the obese hypertensives. WC was found to be positively correlated with QTc among the obese normotensives.

A linear regression analysis was performed to evaluate the independent predictors of QTc. Regression analysis with QTc as a dependent variable showed a linear relationship with WC and WHR among the obese hypertensives (Table 5). Regression analysis with QTc as a dependent variable showed a linear relationship with WC among the obese normotensives (Table 6).

Table 1- Comparison of anthropometric indicators and various other parameters between the three groups

Parameters	***Group1 Obese hypertensives N=15***	**Group 2 Obese normotensives N=15**	**Group 3 nonobese hypertensives N=15**	**P value**
Age (years)	46.00 ± 6.26	46.86 ± 5.16	44.86 ± 6.22	0.652
Height (m)	1.45 ± 0.07	1.43 ± 0.08	1.51 ± 0.08	0.024
Weight (Kg)	68.06 ± 6.04	67.33 ± 6.85	53.46 ± 5.33	<0.001
BMI (kg/m^2)	32.07 ± 1.68	32.71 ± 1.43	23.28 ± 1.31	<0.001
HC (cm)	106.80 ± 4.75	107.80 ± 6.59	97.80 ± 5.01	0.006
WC (cm)	99.60 ± 9.23	97.13 ± 6.22	80.33 ± 4.67	0.000
WHR	0.92 ± 0.05	0.90 ± 0.03	0.82 ± 0.03	0.000
Systolic Bp(mmHg)	156 ± 6.13	115 ± 4.48	154 ± 5.05	0.000
Diastolic Bp(mmHg)	102 ± 7.55	72 ± 7.16	101 ± 6.87	0.000
QT (millisec)	364.40 ± 27.06	370.47 ± 34.50	324.27 ± 53.19	0.05
QTc (millisec)	465.53 ± 34.49	434.13 ± 21.71	375.93 ± 57.52	0.00

Data are presented as Mean ±SD. BMI=Body Mass Index, HC=Hip circumference, WC=Waist Circumference, WHR=Waist Hip Ratio, Bp=Blood pressure. * $p<0.05$ is considered statistically significant.

Table 2- Correlation of QTc with various parameters among the obese hypertensives

Parameters (n=15)	P value	R value
BMI	0.01*	0.635
WC	0.00*	0.967
WHR	0.00*	0.869

Pearson correlation analysis was performed to analyze the data. * p<0.05 is considered statistically significant. BMI=Body Mass Index, HC=Hip circumference, WC=Waist Circumference, WHR=Waist Hip Ratio

Table 3- Correlation of QTc with various parameters among the obese normotensives

Parameters (n=15)	P value	R value
BMI	0.95	0.017
WC	0.00*	0.910
WHR	0.85	0.050

Pearson correlation analysis was performed to analyze the data. * p<0.05 is considered statistically significant. BMI=Body Mass Index, HC=Hip circumference, WC=Waist Circumference, WHR=Waist Hip Ratio

Table 4- Correlation of QTc with various parameters among the obese hypertensives

Parameters (n=15)	P value	R value
BMI	0.35	0.255
WC	0.63	0.134
WHR	0.28	0.255

Pearson correlation analysis was performed to analyze the data. * p<0.05 is considered statistically significant. BMI=Body Mass Index, HC=Hip circumference, WC=Waist Circumference, WHR=Waist Hip Ratio

Table 5: Linear regression analysis to find the effect of QTc on WC, WHR and BMI among the obese hypertensives cases

Independent variables	Non standardized coefficients B value	Standardized coefficients β	P value
BMI	*13.14*	*0.635*	0.07
WC	*3.64*	*0.967*	*0.00**
WHR	*51.68*	*0.869*	*0.00**

* p<0.05 is considered statistically significant. BMI=Body Mass Index, HC=Hip circumference, WC=Waist Circumference, WHR=Waist Hip Ratio

Table 6: Linear regression analysis to find the effect of QTc on WC, WHR and BMI among the obese normotensives cases

Independent variables	Non standardized coefficients B value	Standardized coefficients β	P value
BMI	*0.265*	*0.017*	*0.95*
WC	*3.175*	*0.910*	*0.00**
WHR	*29.75*	*0.050*	*0.85*

* p<0.05 is considered statistically significant. BMI=Body Mass Index, WC=Waist Circumference, WHR=Waist Hip Ratio

Discussion

Ventricular repolarization is most commonly assessed electrocardiographically by measuring the corrected QT interval (QTc) and either QT or QTc dispersion.[9] Known causes of

QTc prolongation include the congenital long QT syndromes, the Brugada syndrome, electrolyte disturbances (hypokalemia, hypomagnesemia, hypocalcemia), selected drugs (e.g., certain anti-arrhythmic drugs, phenothiazines, tricyclic antidepressants, erythromycin in combination with certain antihistamines, pentamidine, and certain anti-malarials), liquid protein and starvation diets, hypothyroidism, central nervous system lesions, severe bradycardia, mitral valve prolapse, acute myocardial

infarction, and possibly obstructive sleep apnea. [10, 11]

Multiple studies of obese subjects have reported prolonged QTc, suggesting an association between obesity and delayed ventricular repolarization. Seyfeli *et al*. reported that mean QTc and QTc dispersion values were significantly longer/greater in 42 obese than in 25 lean women.[12] Study by Rita M showed a significant, but weak positive correlation between BMI and QTc in 50 normotensive severely obese subjects.[13] BMI correlated positively and significantly with QTc and QTc dispersion in Seyfeli's study and independently predicted QTc.[12] In a study of 122 men including 59 with uncomplicated obesity and 63 lean controls QTc correlated positively and significantly with BMI and waist circumference.[5]

QT interval prolongation is associated with ventricular arrhythmia and sudden cardiac death.[14] It has also been shown to be associated with increased mortality in ischemic heart disease and diabetic nephropathy.[15, 16] Obesity has been reported as the cause of QT interval prolongation. However, studies conducted in patients with uncomplicated obesity have demonstrated no effect of weight gain on cardiac repolarization.[17]

Pontrolli AE suggested that QTc was higher in morbidly obese subjects, with or without hypertension, and in lean hypertensive subjects than in lean controls. Sustained and prolonged haemodynamic burden is required to induce structural changes of the left ventricle as it happens in long-lasting obesity and in hypertension.[18]

The standard clinical correction is to use the Bazett's formula which calculates the heart rate-corrected QT interval of QTC with the formula of $QTC = QT/\sqrt{RR}$.[19] QT interval in women is longer compared with men because of the effect of sex hormones on cardiac electrophysiology.[20]

Linear regression analysis also showed a linear relationship between WC and QTc among obese hypertensives and normotensives and also a linear relationship between WHR and QTc among obese hypertensives. This indicates that abdominal obesity can be used to predict changes in QTc.

Increased QTc dispersion can therefore serve as non-invasive marker of increased cardiovascular risk and can therefore be an effective screening for reduction of cardiovascular morbidity and mortality in obese individuals. Therefore, aggressive control of blood pressure, appropriate lifestyle modification campaign may be the best form of preventive strategy to reduce the frequency of prolonged QTc in subjects with obesity and hypertension

From the present study, it is evident that abdominal obesity can cause significant increase in QTc, which indicates that WC and WHR can be used as parameters to predict changes in QTc. A large-scale study is warranted to further validate the findings of the present study.

There are multiple limitations to this study. These include the small sample size and the absence of data derived from newer measures of ventricular repolarization such as transmural dispersion of repolarization. Polysomnography was not performed in most patients; thus, we were unable to assess the role of obstructive sleep apnea on ventricular repolarization in normotensive severely obese patients. Several metabolic factors that might influence ventricular repolarization like plasma insulin levels, free fatty acids, and catecholamines were not measured.

Conclusion

This study indicates that obesity is an important predictor of QTc prolongation than blood pressure. Waist circumference and WHR which reflects abdominal obesity have greater association with QTc prolongation. QTc can be used in routine screening of the obese and hypertensive patients for cardiac complications and prognosis.

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