ORIGINAL ARTICLE

COMPARISON OF ARTERIAL STIFFNESS INDEX AND TPE/QT RATIO IN NORMOTENSIVE, PREHYPERTENSIVE AND HYPERTENSIVE SUBJECTS

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Background: When the blood pressure rises, there is decrease in coronary blood flow to the endocardium and mid-myocardial cells, thereby slowing repolarization in these areas. The major underlying pathophysiology in essential hypertension is arterial stiffness. In this study we compared arterial stiffness index (ASI), T wave peak to end interval (Tpe) and Q to T wave (QT) interval on ECG tracings. Methods: It was a cross-sectional study. Written informed consent was obtained from all subjects. Using non-probability convenience sampling a total of ninety (90) male subjects aged 35–55 years were selected and divided into 3 equal groups, i.e., normotensive, prehypertensive and hypertensive. Blood pressure was measured with mercury sphygmomanometer according to the standard protocols. The ASI was calculated from digital volume pulse recorded by photoplethysmography via iWorx-214; physiological interface system. The 12-lead surface EGG was recorded with Delta-1 Plus digital ECG machine. The ECG tracings were scanned and saved in the computer. QTc, cQTp and cTpe/QTc ratio was calculated in normotensive, prehypertensive and hypertensive middle-aged men. These intervals were corrected by Bazzet’s formulae. Results: The ASI was significantly different (\( p<0.0001 \)) amongst the groups along with QTc and cQTp. However, cTpe intervals and cTpe/QTc were comparable amongst the groups. Conclusion: ASI is major culprit in pathophysiology of hypertension. QTc and cQTp interval are more robust parameter than other ECG markers in detecting transmural dispersion of repolarization in prehypertensive and hypertensive subjects.

Keywords: Electrocardiography, Prehypertension, hypertension, arterial stiffness, coronary blood flow, photoplethysmography

INTRODUCTION

Hypertension is an ever rising medical and public health issue which has huge social and economic burden. The measurement of arterial stiffness index (ASI) has been proposed to be a useful non-invasive tool for the cardiovascular risk evaluation because it can identify early target organ damage. The arterial wall stiffness determined by analysis of digital volume pulse contour is a simple and noninvasive tool for assessing arterial stiffness. There has been strong evidence that the stiffness index score derived by this technique is comparable to the arterial stiffness determined by pulse-wave velocity which is the gold standard marker.1 ASI may serve as a noninvasive tool for finding out the patients at risk of stroke, coronary artery disease and heart failure. It has been documented to be more sensitive tool in risk stratification for cardiovascular diseases (CVD) in comparison to plasma glucose, total cholesterol, and waist to hip ratio in apparently healthy population.2 Thus, ASI may serve important role in preventive medicine. The ventricular arrhythmias have been associated with a higher pulse wave velocity and ASI independent of age or blood pressure in patients with hypertension.3

The electrocardiographic T wave is formed during ventricular repolarization. The interval from the peak to end of T wave (Tpe) has been proposed to represent transmural dispersion of repolarization. The increased cTpe interval and cTpe/QTc ratio has been associated with malignant ventricular arrhythmias in both inherited and acquired CVD.4 Recently, several studies have suggested that cTpe may correspond to the transmural dispersion of repolarization. The increased cTpe interval and cTpe/QTc ratios are associated with malignant ventricular arrhythmias and cardiovascular mortality.5

T-wave is the most sensitive wave of ECG and represents the repolarization phase of ventricles. In case of ischemia of the ventricles, it is the T wave that manifests changes at earliest. It may serve as a sensitive marker to depict early changes in electrical activity of the heart which may result from arterial stiffening and hypertension. From the basic principles of ECG, it is evident that T and R waves can only be in concordance if depolarization and the repolarization waves travel in opposite directions at least in some parts of the ventricle. Hence the cells that activate first are supposed to repolarize last to produce a T wave of the same polarity as that of the R wave. Under normal physiological conditions, peak of the upright T wave determines the complete repolarization of epicardium and the end of T wave describes repolarization of the (midmyocardium)
M region. The Tpe has been proposed to determine the estimate of the transmural dispersion of repolarization. The epicardium starts repolarization ahead of the remaining depolarized ventricles, thus the voltage difference between the epicardium and the M region progressively increases, giving rise to the ascending limb of the T wave. The voltage gradient between the M region and epicardium is at maximum when the epicardium is fully repolarized and the peak of the T wave on ECG denotes this point. As the endocardium also starts repolarizing, the voltage gradient decreases, which limits the amplitude of the T wave and contributes to the initial part of the descending limb of the T wave. The gradient continues to decline as the M cells repolarize which are the last to repolarize as they have the longest action potential duration. All gradients are extinguished when the M cells are fully repolarized and the T waves returns to the baseline.6

The septum and the endocardium, which depolarize first are believed to repolarize last because the septum and other endocardial areas have prolonged contraction than the external surfaces of the heart. It has been postulated that the high blood pressure inside the ventricles during contraction is responsible for this sequence of repolarization. It has been proposed that high blood pressure greatly reduces coronary blood flow to the endocardium and M cells, therefore slowing repolarization in these areas. Thus, epicardium of the ventricles repolarize ahead of inner surface, the positive end of overall ventricular vector during repolarization is towards the apex of the heart and T wave is in the same direction as normal QRS resultant vector.7

The objectives of this study were to compare Arterial Stiffness Index in prehypertensive and hypertensive subjects, especially in middle aged men, and to measure ventricular repolarization parameters, i.e., QTc, cQTp and cTpe/QTc ratio in ECG tracings which may detect the early electrical changes in prehypertensive and hypertensive subjects.

SUBJECTS AND METHODS

This study was carried out at Department of Physiology, Army Medical College, in collaboration with Electrophysiology Department of National Institute of Cardiology, Rawalpindi, Pakistan from Dec 2015 to Dec 2016. It was a cross-sectional study. Thirty male subjects aged 35–55 years were selected in each of normotensive, prehypertensive and hypertensive group by non-probability, convenience sampling.

Around 1,000 subjects were interviewed. Subjects having any allergic disease, fever, or taking any medications for at least last two weeks were excluded from the study. Those who had diabetes, chronic inflammatory disease or any prolonged illness were also excluded. The study started after approval from Ethical Review Committee, Army Medical College and Centre for Research in Experimental and Applied Medicine (CREAM). After informed consent, the subjects’ particulars were recorded and detailed medical history was inquired.

Blood pressure was measured by auscultatory method with mercury sphygmomanometer. In order to exclude diabetes mellitus blood sugar was checked with glucometer. Photoplethesmograph was placed on the volar surface of distal segment of middle finger and digital volume pulse (DVP) was recorded by Human/Animal Physiology interface system iWorx-214. The recorded data was analyzed using LabScribe software and reflection time was calculated by placing cursor on the two peaks of DVP. The arterial stiffness index was calculated as ASI=Height (meters)/Reflection time (seconds).

The scanned copies of all electrocardiographic recordings were saved on the computer. The QT, QTp, and RR intervals in leads V4–V6 were measured by using screen callipers. The screen calliper was calibrated after zooming five times (5×) the scanned file of ECG recording. Then QT, QTp, and RR interval were measured in milliseconds. The Tpe was calculated by subtracting QTp from QT. By using Bazett’s formulae, corrected QTc, cQTp and cTpe were figured out as QTc=QT/√RR (in seconds). The cTpe/QTc ratio was calculated by plotting the cTpe and QTc values.

Statistical analysis was performed using SPSS-20. One-way ANOVA was applied followed by Post-hoc Tukey’s test to compare the ASI and ECG parameters like cQT, cQTp, cTpe, and cTpe/QTc in normotensive, prehypertensive and hypertensive subjects, and p<0.05 was considered statistically significant.

RESULTS

The ASI and ECG parameters (QTc, cQTp, cTpe, cTpe/QTc) were compared amongst normotensive, prehypertensive and hypertensive groups by one-way ANOVA (Table-1).

It revealed statistically significant difference of ASI, QTc and cQTp intervals amongst the groups. The differences of variables between the groups calculated by Post-hoc Tukey’s test are presented in Table-2.

Table-1: Comparison of study variables among the three groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASI</td>
<td>6.67±0.32</td>
<td>7.85±0.62</td>
<td>12.19±2.62</td>
<td>0.0001</td>
</tr>
<tr>
<td>QTc (ms)</td>
<td>413±25</td>
<td>430±27</td>
<td>448±29</td>
<td>0.0001</td>
</tr>
<tr>
<td>QTp (ms)</td>
<td>10.03±0.66</td>
<td>10.36±0.71</td>
<td>10.77±0.79</td>
<td>0.001*</td>
</tr>
<tr>
<td>Tpe (ms)</td>
<td>96±16</td>
<td>103±17</td>
<td>108±24</td>
<td>0.07</td>
</tr>
<tr>
<td>Tpe/QTc</td>
<td>0.215±31</td>
<td>0.215±37</td>
<td>0.216±37</td>
<td>0.99</td>
</tr>
</tbody>
</table>

*Significant

ASI: Arterial Stiffness Index; QTc: corrected interval between Q wave and the end of T wave; cQTp: corrected interval between Q wave and the peak of T wave; cTpe: corrected interval between the peak of T wave to its end; ms: millisecond
DISCUSSION

There was a significant difference of ASI between the normotensive, prehypertensive and hypertensive subjects. The raised arterial stiffness results in increased peripheral vascular resistance which has been documented as one of the leading cause of essential hypertension. Different techniques have been employed to measure the ASI in various studies ranging from simple to intricate ones. We have calculated the ASI from the digital volume pulse (DVP) recorded by photoplethysmography in iWorx-214 Human Physiology Interface System. The ASI measured via this technique is simple that can be done in office setting or at the bed-site as compared to other costly and cumbersome methods. The ASI determined by this technique may serve as a sensitive, simple and non-invasive tool for the determination of vascular wall stiffness.

In our study, there was no significant difference in corrected cTpe and cTpe/QTc ratio among the normotensive, prehypertensive and hypertensive groups. However, cQT interval was significantly different amongst the groups. Our results were similar to the study by Mozos et al, in which there was no difference in Tpe and Tpe/QTc ratio among the normotensive and hypertensive subjects without left ventricular hypertrophy (LVH), but cQT and cQTp were significantly different amongst the groups. Our results were also supported by another study in which Tpe interval was comparable in normotensive and non-LVH hypertensive subjects.

Our results are different from the findings of other studies, in which corrected Tpe and Tpe/QT ratio were significantly different in hypertensive patients as compared to prehypertensive and normotensive subjects. The difference in findings may be due to the duration of hypertension in both the studies, and the hypertensive subjects in the study might have left ventricular hypertrophy. The left ventricular hypertrophy, even minimal one, has been associated with increased cTpe and Tpe/QTc ratio.

The QTc interval in the left precordial leads represents the repolarization phase of the left ventricle. In hypertensive patients it was expected that the Tpe interval and Tpe/QT ratio might be prolonged due to the lengthening of the late phase of repolarization across the ventricles.

The myocardium receives its most of the blood supply, during ventricular diastole. During systole, the ventricular walls contract and the blood vessels are collapsed, so blood flow through the coronary vessels is compromised. In hypertension, mean systemic filling pressure and ventricular pressure increase during the late phase of diastolic filling. It causes mechanical stretching of the ventricular walls, and its blood supply is compromised especially in the midmyocardial cells which depolarize at the end. Though, an upward trend was observed in cTpe amongst the normotensive, prehypertensive and hypertensive subjects but there was no statistical difference among the groups. As the cQT interval was associated with BP variables but not with Tpe and Tpe/QTc ratio therefore from it may be hypothesized that Tpe is the index of total dispersion of repolarization which might not determine the transmural dispersion of repolarization. It was expected that there will be change in Tpe interval if it represented the transmural dispersion of repolarization as compared to cQT interval in prehypertension and hypertension without hypertrophy. The prolongation in repolarization results from changes in the transmural dispersion of repolarization due to mechanical effects and the sympathetic stimulation. So, cTpe may not be sensitive enough to detect early changes in dispersion of the repolarization as compared to cQTp and QTc.

The rise in blood pressure has been associated with autonomic imbalance, marked by predominant increase in sympathetic activity in hypertensive patients. Passino et al, argued that increased sympathetic activity might contribute in abnormal ventricular repolarization. In their findings they studied 47 untreated subjects with essential hypertension and thirty five endurance runners, with a similar degree of left ventricular hypertrophy, and found increased plasma nor epinephrine levels and prolonged cQT interval in hypertensive subjects as compared to the endurance athletes. The underlying mechanism was not explained. It may be due to contraction of coronary vasculature especially the intramuscular branches from endocardial and epicardial plexus as a result of increased sympathetic outflow which compromised the blood supply to muscular layers of ventricles. The epicardial and endocardial layers are less effected as compared to the midmyocardial M cells lying in the muscular layers resulting in the heterogeneity of ventricular repolarization due to the silent ischemic changes during the cardiac cycle. It is believed that cQT is a more robust parameter to detect the risk of arrhythmias in hypertensive subjects, especially in early stages of hypertension.

Salles et al, studied various repolarization parameters including cQT, QTp and Tpe in order to determine the prognostic worth of these EGG
parameters in prolonged ventricular repolarization. In 538 hypertensive subjects, the prolonged QTc-interval above 460 ms was associated with higher risk of cardiovascular morbidity and mortality. No other repolarization parameter added to further prognostic information to the prolongation of repolarization duration.\textsuperscript{16} In another study on middle aged elderly men. It was found that QTc, within a normal range, have lesser risk of coronary heart disease.\textsuperscript{17} In uncomplicated hypertensive patients, the QTc prolongation had been associated with increased risk of ischemic heart disease and cardiovascular mortality.\textsuperscript{18} There had been conflicting evidence that the QTc or cTpe were better predictor of ventricular arrhythmias.

**CONCLUSION**

Arterial stiffness detected by ASI is the major culprit in pathophysiology of hypertension. QTc and cTpe are more robust parameter than other ECG markers in detecting transmural dispersion of repolarization in prehypertensive and hypertensive subjects, especially in early stages of hypertension. The Tpe intervals and Tpe/QTc ratio is not altered in the hypertensive subjects at least in early stages of the disease process.

**REFERENCES**


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