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ORIGINAL ARTICLE

QT Dispersion in Hypertensive Nigerians with and without Left Ventricular Hypertrophy

Dispersion de QT chez des Nigerians Hypertendus avec et sans Hypertrophie Ventriculaire

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ABSTRACT

BACKGROUND: **Increased QT dispersion (QTd) has been implicated as a marker of arrhythmogenesis and cardiac death. Paucity of literature on QTd in Nigeria necessitated an inquiry into QTd in adult hypertensive population. This study sought to: (i) compare the QTd values of adult hypertensive subjects with age and sex matched normotensivesubjects and (ii)examine the relationship between QTd and left ventricular hypertrophy (LVH).**

STUDY DESIGN: **One hundred and fifty-one hypertensive patients and 101 age and sex-matched controls were recruited into this study. A resting 12- lead ECG was obtained from all subjects for determination of QTd and ECG LVH using Sokolow Lyon (SL) and Araoye's codes. Echocardiographic LVH was determined for 60 hypertensive subjects and 60 age/sex matched controls.**

RESULTS: **Hypertensive subjects had higher mean QTd than the controls (65.6 ± 28.1ms vs 38.7 ± 11.3 ms, p< 0.0001). QTd of hypertensives with ECG LVH was significantly higher than those without ECG LVH (Araoye: 71.5 ± 22.0ms vs 62.2 ±24.1ms, p = 0.02, SL; 72.0 ±24.4ms vs 61.6±23.1ms p = 0.009). Similarly the QTd of hypertensives with echocardiographic LVH (72.6 ± 21.3ms) was higher than those without (60.1 ± 22.2ms) but did not achieve statistical significance (p = 0.085).**

CONCLUSIONS: **Hypertension with or without ECG LVH is associated with significantly increased QTd. Echocardiographic LVH is associated with a non significant increase in QTd in hypertensive subjects. WAJM 2013; 32(1): 57–61.**

Keywords: **QT dispersion left ventricular hypertrophy, Nigerians, hypertensives.**

RÉSUMÉ

CONTEXTE: L'accentuation de la dispersion de QT (dQT) a été reconnue comme un marqueur d'arythmogènèse et d'infarctus du myocarde. La rareté de la littérature sur la dQT au Nigeria avait entrainé la nécessité de s'enquérir de la dQT au sein d'une population d'adultes hypertendus. Cette étude visait à: (i) comparer les valeurs de dQT de sujets adultes hypertendus avec ceux de sujets normotendus avec croisement selon l'âge et le sexe et (ii) examiner les relations entre dQT et hypertophie ventriculaire gauche (HVG)

SCHEMAS D'ÉTUDE: Cent cinquante et un patients hypertendus et 101 témoins croisés selon l'âge et le sexe ont été inclus dans cette étude. Un ECG à 12 signaux électriques au repos a été réalisé chez tous les sujets pour la détermination de la dQT et d'une HVG électrique en utilisant les Indices de Sokolow Lyon (SL) et de Araoye's. Une HVG échocardiographique a été déterminée chez 60 sujets hypertendus et 60 témoins croisés par âge/sexe.

RÉSULTATS: Les sujets hypertendus avaient une plus grande moyenne de dQT comparés aux témoins (65,6 ± 28,1ms vs 38,7 ± 11,3 ms, p< 0.0001). La dQT chez les hypertendus avec une HVG électrique était significativement plus élevée que chez ceux sans HVG électrique (Araoye: 71,5 ± 22,0ms vs 62,2 ±24,1ms, p = 0,02, SL; 72,0 ±24,4ms vs 61,6±23,1ms p = 0,009). De façon similaire, la dQT chez les hypertendus avec HVG électrique (72,6 ± 21,3ms) était plus grande que celle de ceux sans HVG électrique (60,1 ± 22,2ms)mais la différence n'était pas statistiquement significative (p = 0,085).

CONCLUSIONS: L'hypertension atérielle avec ou sans HVG électrique est associée à une augmentation significative de la dQT. L'HVG Echocardiographique est associée à une aumentation non significative de la dQT chez les patients hypertendus. **WAJM 2013; 32(1): 57–61.**

Mots clés: dispersion de QT, Hypertrophie Ventriculaire Gauche, Nigerians, hypertensifs.

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Abbreviations: ANOVA, Analysis of variance; **ASE,** American Society of Echocardiography; **CV,** Cardiovascular; **ECG,** Electrocardiogram; **LVMI,** Left ventricular mass index; **LVH,** Left ventricular hypertrophy; **LVIDs,** Left ventricular internal diameter in systole; **LVIDd,** Left ventricular internal diameter in diastole; **QTd,** QT dispersion; **SL, Sokolow Lyon.**

INTRODUCTION

Hypertension is a potent and the leading cardiovascular (CV) risk factor for morbidity and mortality worldwide.[1] Hypertensive end organ damage include a multitude of functional and structural cardiac changes referred to as hypertensive heart disease. Left ventricular hypertrophy (LVH), a form of hypertensive heart disease is of a central importance.

LVH is a compensatory mechanism for ventricular overload. It is an independent risk factor for CV morbidity and mortality in hypertensive and normotensive individuals.[2, 3] LVH has been associated with increased frequency of ventricular arrhythmias and sudden cardiac death.[4] This is thought to be due in part to the induction of pro-arrhythmic repolarisation changes caused by the imbalance between the myocytes and the interstitium of the myocardial skeletal structure occurring in pathological LVH.[4] QT dispersion is defined as the maximal interlead difference in the QT intervals in a surface resting electrocardiogram.[5] It is an index of myocardial repolarisation in homogeneity.[5] Increased QT dispersion is a strong and independent risk factor of cardiac mortality and malignant ventricular arrhythmias in hypertension.[6,7] Hypertensive subjects have been reported to have increased QTd[7–9] with presence of LVH further increasing QTd.[8–11]

Owing to the paucity of information on QTd among Nigerians, this study sought to evaluate QT dispersion in hypertensive Nigerians. The aims of this study are: (i) To compare the QTd values of adult hypertensive subjects with age and sex matched normotensivesubjects (ii) To examine the relationship between QTd and electrocardiographic and echocardiographic LVH in hypertensive subjects.

SUBJECTS, MATERIALS AND METHODS

Study locations were outpatient clinics. The participants were 151 consecutive hypertensive subjects and 101 age and sex matched apparently healthy controls. Hypertension was defined as blood pressure persistently $\geq$ 140/90 mmHg and/or being on antihypertensive therapy.[12]

Inclusion criteria for the hypertensive subjects and controls were age $\geq$18 years and fasting blood sugar < 7mmol/l. Exclusion criteria for the hypertensives and controls were presence of chronic medical illness such as heart failure, ischaemic heart disease, renal failure, diabetes mellitus and nervous system disorder known to affect QT interval, and intake of drugs known to potentially influence QT duration (e.g. ACE inhibitors, angiotensin receptor blockers, beta- adrenergic blockers, statins, spironolactone, calcium channel blockers, macrolide antibiotics, halofantrine), presence of sustained non-sinus rhythms (e.g. atrial fibrillation), and intraventricular conduction defects. Subjects with ECG in which the end of T wave cannot be reliably determined and/ orin which QT interval from less than 8 leads can be recorded were excluded. Subjects with suboptimal echocardiographic windows were excluded from echocardiographic assessment.

Esaote P80 Power electrocardiograph machine was used to obtain a resting simultaneous 12 lead electrocardiogram (ECG) and a standard lead II rhythm strip from all the subjects at a paper speed of 25mms^{-1} with the machine control set at standard response. A minimum of three cardiac cycles were recorded for each lead.

QT intervals of 2–3 consecutive cardiac cycles in each lead were measured manually and averaged. QT interval was defined as the interval between the first deflection of the QRS complex to the point of T wave offset (i.e. the point of the return of the terminal T wave to the isoelectric TP baseline).[7] In the presence of U wave interrupting the T wave, the nadir between the T and U waves was used to define the point of T wave offset. QT dispersion was defined as the difference between the shortest (QT min) and longest (QT max) average QT interval in each electrocardiogram.[7] Abnormal QT dispersion was defined as QTd > the mean QTd + 2SD of the controls in this study.

Each QT interval was corrected for subjects' heart rate using Bazett's formula:[13] $QTc = QTo/\sqrt{RR}$ where: QTc is the corrected QT interval, QTo is the observed QT interval in milliseconds,RR is the RR interval in milliseconds. Prolonged QTc was taken as QTc greater than the mean QTc + 2SD of the controls of each gender in this study.

ECG LVH was diagnosed using the Araoye's proposed criteria for LVH in the blacks[14] and the Sokolow - Lyon criteria[15]. In addition, transthoracic echocardiography was performed on the first consecutive 60 hypertensive subjects and 60 age and sex matched controls using Hewlett Packard Sonos 2000 machine. According to the American Society of Echocardiography (ASE) recommendations,[16] the following measurements were obtained using the leading edge to leading edge method: left ventricular internal diameter in diastole (LVIDd), left ventricular internal diameter in systole (LVIDs), interventricular septal thickness in diastole (IVST) and left ventricular posterior wall thickness in diastole (PWT). Left ventricular mass index (LVMI) was derived using the ASE formulastated below:[16]

Estimated LVMI (g/m^2) = $0.80[1.04(LVIDD + PWT + IVST)^3 - LVIDD)^3] = 0.6g/BSA$ Echocardiographic LVH was defined as LVMI of > $110g/m^2$ and >$134gm/m^2$ in women and men respectively.[17]

The SPSS 17.0 statistical software was used for data analysis. The data obtained were expressed as means and proportions. Statistical significance of variables was estimated using chi-square for categorical variables and student t-test for continuous variables. Analysis of variance (ANOVA) was used when the means of more than two groups were compared. Pearson's correlation coefficient analysiswas performed and variables that demonstrated significant positive relationship to QT dispersion were then entered into a multiple regressionanalysis. Results were considered significant if $p < 0.05$.

RESULTS

Study participants were 151 hypertensive subjects and 101 age and sex-matched controls. 16.6% (n=25) of the hypertensive subjects were untreated. Table 1 shows the clinical characteristics of the study group. Echocardiographic and ECG parameters of study group are shown in Table 2. The hypertensives had

Table 1: ClinicalCharacteristics of the Study Group

Variable	Mean ± SD or N (%)		
	Hypertensives	Controls	p-value
Age (years)	53.3 ± 13.3	53.0 ± 13.5	0.81
Age echo** (years)	47.7±11.4	47.4±11.1	0.9
Male (N%)	47 (31.1%)	34 (33.7%)	0.67
Male echo(N%)	19 (32%)	20 (33%)	0.85
BMI (kg/m^2)	28.2 ± 5.9	26.5 ± 4.7	0.02
Mean SBP (mmHg)	155.3 ± 24.7	118.7 ± 9.5	0.002
Mean DBP (mmHg)	93.2 ± 13.0	74.1 ± 7.7	0.00*
MAP (mmHg)	114 ± 15.3	87.6 ± 8.6	0.00*
Heart rate (beats/min)	79.1±15.1	73.3±10.1	0.001

p < 0.05, **age of subpopulation with echocardiograms, **SBP, Systolic blood pressure, **DBP,** Diastolic blood pressure; **BMI,** Body mass index.*

Table 2: ECG and Echocardiographic Characteristics of 60 Hypertensive Patients and 60 Age and Sex-matched Controls

Variable	Mean ± 2SD or N (%)		
	Hypertensives	Controls	p-value
QTc (M & F)	433±28.4	417.9±23.6	<0.00
QTc (F)	438.0 ± 29.3	425.7 ± 21.7	0.004
QTc (M)	421.8 ± 23.0	402.7 ± 19.8	<0.00*
Prolonged QTc (N %)	59 (39%)	9 (9%)	<0.00*
QTd (ms)	65.6±28.1	38.7±11.3	<0.00*
Abnormal QTd (N %)	54(35.8%)	16(15.8%)	<0.02
LVH - Araoye (N %)	56 (37.1%)	14 (13.9%)	<0.00*
LVH -Sokolow-Lyon (N %)	59 (39.1 %)	12 (11.9%)	<0.00*
LVM (gm)	182.35 ± 68.33	153.03 ± 35.91	0.004
LVMI (g/m^2)	101.01 ± 33.08	84.93 ±18.64	0.01
Echo LVH (N %)	12 (20%)	2 (3.3%)	0.008

**p < 0.05 LVM, Left ventricular mass; LVMI, Left ventricular mass index; LVH, Left ventricular hypertrophy; M, males, F, females*

Table 3: QT Dispersion According to LVH status in hypertensive subjects

LVH Status	A (n=151) QTd ± SD (ms)	B (n=151) QTd ± SD (ms)	C (n=60) QTd ± SD (ms)
LVH	72.0±24.4	71.5 ± 22.0	72.6 ± 21.3
No LVH	61.6 ± 23.1	62.2 ± 24.1	60.1 ± 22.2
p- value	0.009	0.02	0.085

LVH, Left ventricular hypertrophy; A, Araoye's code; B, Sokolow-Lyon criteria, C, Echocardiographic LVH

a significantly higher mean QTd than the controls (65.6 ± 28.1ms vs 38.7±11.3 ms, p<0.0001). The proportion of hypertensives (63.6%, n= 96) and controls (113.9%, n= 14) having abnormal QTd were also significantly different (p<0.0001). Table 2 also show a significantly higher proportion of hypertensives having ECG and echocardiographic LVH when compared with the controls (p < 0.0001 and p = 0.008 respectively). Table 3 summarises the mean QTd of the hypertensives according to LVH status using Araoye's code (A), Sokolow-Lyon criteria (B) and echocardiography(C). Hypertensives with LVH had higher mean QTd values than those without LVH. However only the association of QTd with ECG LVH attained statistical significance (Araoye: p=0.02, Sokolow-Lyon: p= 0.009, Echocardiography: p = 0.085). Table 4 shows the Pearson correlation coefficient between QTd and some selected parameters. None of the parameters that achieved significant correlation with QTd (i.e. age and QTc) attained significance when entered into multiple regression analysis.

Table 4: Pearson's Correlation Coefficient between QTd and some Selected Variables in the Hypertensive Subjects

Parameter	r	p-value
Age	0.18	0.03*
BMI	–0.03	0.71
SBP	0.13	0.13
DBP	0.03	0.71
MAP	0.07	0.35
HR	–0.11	0.17
QTc	0.18	0.03*
LVM	0.15	0.42
LVMI	0.15	0.25

BMI, Body mass index; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; MAP, Mean arterial blood pressure; HR, Heart rate; QTc-Corrected QT interval, LVM, Left ventricular mass; LVM, Left ventricular mass index.

DISCUSSION

This study demonstrated a significantly higher QT dispersion in the hypertensive subjects than the controls (p< 0.000001). This is similar to previous reports.[8–10] The adaptive structural changes in the hypertensive myocardium with a consequent structural and electrical inhomogeneity of the myocardium may be partly responsible for this.[8] In addition to this is a hypothesis which suggests that increased afterload which is associated with hypertension working through a mechano-electric feedback on the heart causes pronounced alterations in the durations of the myocardial action potentials.[18] The later may explain the higher QTd values observed in the hypertensive subjects irrespective of

their LVH status. A large variability was observed in the mean QTd values of the hypertensive subjects in the above studies.[9–11]The mean QTd value for the hypertensives in the current study (65.6 ± 28.1ms) is different from the values observed by Vilas-Boas *et al.*,[8] Zoghi *et al.*[10] and Sani *et al.*[11] respectively in the hypertensive populations in their studies. These variations observed in the mean QTd values in these studies[10, 12, 13] may be due to methodological issues such as mode of QT measurement, definition of T wave offset, paper speed at which the ECGs are recorded and interobserver reproducibility, which are associated with the measurement of QT dispersion.[7] Peculiarities of the Negroid myocardium such as higher left ventricular mass, earlier onset of hypertensive heart disease, and higher ECG voltages when compared with that of the white race may also contribute to the differences observed in the mean QTd values of various studies.[14, 19]

There is a significant association between QTd and ECG LVH amongst the hypertensive subjects. This is consonance with the Clarkson *et al.*[9] and Oikarinen *et al.*[20] who documented a significant positive association between QTd and ECG LVH among hypertensives.

Echocardiographic LVH and LVMI were independent of QTd among the hypertensives in this study. This trend was also demonstrated by Vilas-Boas *et al.*[8] who showed that QTd correlated positively but insignificantly with LVMI. It is however at variance with data from Clarkson *et al.*[9] and Davey *et al.*[21] which noted a significant and positive correlation. The lower proportion of untreated hypertensives in our study (16.6%, n=25) in contrast to all (100%) in the above studies by Clarkson *et al.*[9] and Davey *et al.*[21] may also be contributory to this finding.

ECG criteria for LVH determination have low sensitivity and high specificity.[22,23]This results in the limitation of these criteria to the detection of only the extreme end of the LVH spectrum. Thus the QTd values obtained for hypertensives with ECG LVH is most likely that of only subjects with severe LVH. On the other hand, echocardiography being a more sensitive method of LVH determination will detect mild to severe cases of LVH.[23] Hence the QTd values obtained for subjects with echocardiographic LVH represent that of hypertensives with mild to severe LVH. This association between high QTd values and ECG LVH (a marker of severe LVH) is consistent with Sani *et al.*[11] who demonstrated that increased QTd is found in hypertensives with more severe LVH.

ECG LVH criteria estimate LVM by measuring abnormal ventricular electrophysiology while echocardiography directly estimates LVM. The fact that QTd and ECG LVH are measures of changes in the electrical properties of the myocardium may explain the significant association of QTd with ECG LVH and not echocardiographic LVH. The smaller population of subjects in this study with echocardiographic LVH assessment (n=60) when compared with those with ECG LVH assessment (n=151) may also explain the significant association of QTd with ECG but not echocardiographic LVH. This is may be likely considering the tendency towards significance (p= 0.085) of QTd in hypertensives with LVH in this study (Table 3). Multivariate analysis in our study demonstrated insignificant relationship between QTd and age. This is agreement with the findings of Saadeh[24] among hypertensives, Macfarlane *et al.*[25] in apparently normal population and Tsagalou *et al.*[26] in heart failure patients.

We have demonstrated in this study that hypertension with or without LVH cause an increase in QT dispersion with the presence of ECG LVH causing even a greater increase. QTd is non-invasive, low-cost and easily obtained from routine ECG. QTd measurement using the manual method may provide additional tool for risk stratification in hypertensives especially in a resource poor country such as Nigeria.

A limitation of this study is that the speed of the standard 12 – lead ECG recordings in clinical practice i.e. 25mms^{-1} was used. QT interval measurements are more reproducible at faster paper speed recordings.[7]

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