Prolonged QTc interval and its relationship to left ventricular hypertrophy and left ventricular ejection fraction in hypertensive patients

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Abstract

Objective: The study aimed to determine the prevalence of prolonged QTc interval in hypertensive patients and investigate its relationship and correlation with left ventricular hypertrophy and left ventricular ejection fraction (EF) in hypertensive patients. **Subjects and Methods:** This study is a cross-sectional descriptive study. The subjects were patients admitted to the Cardiology Department of Hue University of Medicine and Pharmacy Hospital from February 2020 to February 2021, diagnosed with hypertension according to the VNHA 2018 guidelines. The patients were divided into two groups: Group 1 with prolonged QTc and Group 2 with normal QTc. Prolonged QTc was defined as QTc >450ms in males and >460ms in females. All patients underwent echocardiography to assess left ventricular hypertrophy and left ventricular ejection fraction (EF), and comparisons were made between the two groups. A p-value <0.05 was considered statistically significant. **Results:** A total of 133 patients were included in the study, with males accounting for 50.4%. Among them, 41 cases (30.8%) had a prolonged QTc interval, while 92 cases (69.2%) had a normal QTc interval. Patients in the prolonged QTc group had significantly lower ejection fraction and fractional shortening (Fs), higher left ventricular mass index (LVMI), and greater end-diastolic volume (EDV) and end-systolic volume (ESV) compared to those in the normal QTc group. QTc was negatively correlated with EF and Fs and positively correlated with ESV and Ds. Furthermore, the prolonged QTc group had a higher prevalence of heart failure, with statistically significant clinical symptoms of heart failure such as edema, dyspnea, and tachycardia. **Conclusion:** The study indicates that prolonged QTc interval has a relatively high prevalence among hypertensive patients. Prolonged QTc is associated with left ventricular hypertrophy and left ventricular ejection fraction in hypertensive patients.

Keywords: *QTc interval; hypertension; left ventricular hypertrophy; left ventricular ejection fraction.*

1. INTRODUCTION

Hypertension (HTN) is the most common modifiable cardiovascular risk factor. The prevalence of hypertension is increasing and is becoming younger in age. Many studies have shown that a prolonged corrected QT interval (QTc) on the electrocardiogram (ECG) is associated with an increased risk of cardiovascular mortality, all-cause mortality, and the risk of ischemic heart disease in hypertensive patients [1], [2], [3]. Research has demonstrated that hypertension leads to left ventricular hypertrophy (LVH), which alters conduction and causes ventricular repolarization abnormalities, resulting in prolonged QT intervals on resting ECG in hypertensive heart disease [4]. Normally, the heart functions as a coordinated muscle to contract and relax, pumping blood to nourish the body, regulated by the heart's autonomic nodes to control heart rate and rhythm. When the QTc interval is prolonged, it extends the relative refractory period of the action potential, disrupting the timing of each heartbeat and triggering arrhythmias. This is the cause of ventricular arrhythmias, sudden cardiac death, stroke, and mortality in hypertensive patients [2], [3].

With the aim of investigating the relationship between prolonged QTc interval, left ventricular hypertrophy, and left ventricular ejection fraction (EF) in hypertensive patients, we conducted this study with the objective to: identify prolonged QTc in hypertensive patients and evaluate its correlation with left ventricular hypertrophy and left ventricular ejection fraction (EF) in this population.

2. STUDY SUBJECTS AND METHODS

Subjects and Methods

This study is a cross-sectional descriptive study. The subjects were patients admitted to the Cardiology Department of Hue University of Medicine and Pharmacy Hospital from February 2020 to February

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2021, diagnosed with hypertension according to the VNHA 2018 guidelines. Subjects were divided into two groups: Group 1: Prolonged QTc; Group 2: Normal QTc.

Data collection

Information collected from patients included name, age, gender, admission diagnosis, clinical symptoms, ECG results, and echocardiographic findings.

Inclusion criteria

Patients with a history of HTN, currently under treatment, patients newly diagnosed with HTN, confirmed through three measurements, hypertension diagnosis criteria follow the 2018 VNHA guidelines: clinic blood pressure (BP) ≥ 140/90 mmHg [5].

Exclusion criteria

Cases where T-wave could not be clearly identified. Patients with arrhythmias such as atrial fibrillation, atrial flutter, or other rhythm disorders. Conditions affecting the QT interval, such as electrolyte imbalances (hypocalcemia, hypokalemia, etc.), or medications like amiodarone, macrolide and quinolone antibiotics, tricyclic antidepressants….

Electrocardiogram (ECG)**:** ECGs were performed using a CP50 12-lead electrocardiograph (Welch Allyn, USA). ECG was measured once at hospital admission for diagnosis. If changes occurred during hospitalization, repeat measurements were performed. ECG parameters analyzed included rhythm, frequency, axis, waves, ST segment, QT and QTc intervals, atrial fibrillation, associated arrhythmias, ventricular hypertrophy, and myocardial ischemia. The diagnostic criteria followed the 2010 VNHA guidelines and the 2014 AHA guidelines. QT and QTc intervals were automatically calculated and printed by the ECG machine to minimize subjective error. Prolonged QTc was defined as >450 ms for males and >460 ms for females.

Echocardiography

Transthoracic echocardiography was performed following the recommendations of the American Society of Echocardiography. Selected indices for assessing left ventricular function included: left atrial diameter (mm), left ventricular ejection fraction (EF,%), fractional shortening (FS,%), left ventricular systolic diameter (Ds, mm), left ventricular diastolic diameter (Dd, mm), left ventricular mass index (LVMI, g/m²), end-systolic volume (ESV), end-diastolic volume (EDV) [6].

Data Analysis

Data were processed using SPSS version 20.0, with $p<0.05$ considered statistically significant.

3. RESULTS

Among the 133 patients, 67 were male, accounting for 50.4%. Group 1: 41 patients (30.8%) had prolonged QTc intervals. Group 2: 92 patients (69.2%) had normal QTc intervals. The mean age was 69.69 ± 11.99 years. There was a significant difference in the mean heart rate between the two groups (p=0.001). Symptoms such as dyspnea, limb edema, and heart failure also showed statistically significant differences between the two groups (p<0.05).

Table 1. General characteristics of study subjects

Characteristics	Total (N=133)	Group 1 (n=41; 30.8%)	Group 2 (n=92; 69.2%)	p
Male (n, %)	67 (50.4%)	18 (43.9%)	49 (53.3%)	0.319
Male to Female Ratio	67:66	18:23	49:43	0.319
Mean age	69.69 ± 11.99	72.17 ± 14.14	68.59 ± 10.80	0.153
SBP (mmHg)	148.69 ± 25.50	149.20 ± 20.35	147.56 ± 34.46	0.780
DBP (mmHg)	85.34 ± 14.59	85.65 ± 13.03	84.63 ± 17.76	0.743
Heart rate (bpm)	76.75 ± 14.68	82.76 ± 14.50	74.08 ± 14.30	**0.001**
Edema (%)	25 (18.80)	12 (29.27)	13 (14.13)	**0.039**
Dyspnea (%)	15 (11.29)	8 (19.51)	7 (7.61)	**0.045**
Heart failure (%)	17 (12.78)	11 (26.83)	6 (6.52)	**0.001**

SBP (systolic blood pressure), DBP (diastolic blood pressure).

The average QTc interval was 445.53 ± 36.8 ms, with the values for the two groups being 484.88 ± 25.41 ms for Group 1 and 427.99 ± 22.46 ms for Group 2, showing a statistically significant difference (p<0.001). There was no significant difference in the mean PR interval between the two groups (p=0.100) (Table 2).

Table 2. Electrocardiographic characteristics of the study subjects

ECG Characteristics	Total (N=133)	Group 1 (n=41)	Group 2 (n=92)	p
QTc interval (ms)	445.53 ± 36.48	484.88 ± 25.41	427.99 ± 21.46	**<0.001**
PR interval (ms)	169.41 ± 27.24	175.24 ±30.82	166.82 ± 25.23	0.100

There was a statistically significant difference in the mean values of LA, EF, Ds, ESV, EDV, FS, and LVMI between the two groups, with p<0.05 (Table 3).

Table 3. Echocardiographic characteristics of study subjects

Parameters	Total (N=133)	Group 1 (n=41)	Group 2 (n=92)	p
LA (mm)	32.91 ± 7.14	34.63 ± 5.31	32.14 ± 7.73	**0.033***
EF (%)	64.65 ± 13.31	57.80 ± 15.72	67.70 ± 10.85	**0.001***
Dd (mm)	49.81 ± 8.34	50.44 ± 7.02	49.74 ± 9.59	0.535
Ds (mm)	32.94 ± 6.94	35.29 ± 9.35	30.99 ± 9.76	**0.019***
ESV	41.93 ± 27.04	55.50 ± 32.33	35.88 ± 21.93	**0.001***
EDV	115.82 ± 43.11	127.37 ± 39.78	110.67 ± 43.74	**0.039***
FS (%)	36.97 ± 8.76	31.63 ± 9.98	39.34 ± 7.00	**0.001***
LVMI (g/m2)	126.84 ± 46.00	144.34 ± 41.83	119.04 ± 45.83	**0.003***

EF, ejection fraction; Dd, diastolic dimension; Ds, systolic dimension; ESV, end systolic volume; EDV, end diastolic volume; FS, fraction shortening; LVMI, left ventricular mass index.

In the group with left ventricular hypertrophy, there was a correlation between left ventricular ejection fraction and fractional shortening with the QTc interval, with p<0.05 (Table 4).

Table 4. Association between EF, Fs, and QTc interval

	Left Ventricular Hypertrophy	QTc Interval (ms)		p
		Prolonged	Normal	
EF (%)	**Yes**	57.12 ± 16.04	65.35 ± 12.40	**0.01***
	No	66.33 ± 7.77	71.04 ± 7.04	0.274
Fs (%)	**Yes**	31.24 ± 10.16	38.46 ± 7.04	**0.001***
	No	36.67 ± 6.60	40.60 ± 6.27	0.303

EF, ejection fraction; FS, fraction shortening.

There was a moderate inverse correlation between the QTc interval and EF, FS (p<0.001). A moderate positive correlation was found between the QTc interval and ESV (p<0.001), and a weak positive correlation was observed between the QTc interval and Ds (p=0.006) (Table 5).

Table 5. Correlation between QTc interval and echocardiographic parameters

Parameters	QTc Interval (ms)	
	r	p
LA (mm)	0.165	0.057
EF (%)	-0.364	**<0.001***
Dd (mm)	0.109	0.211
Ds (mm)	0.236	**0.006***
ESV	0.438	**<0.001***
EDV	0.209	0.16
Fs (%)	-0.366	**<0.001***
LVMI (g/m2)	0.161	0.064

LA, Left atrial diameter (in millimeters); EF, Ejection fraction; Dd; diastolic diameter; Ds, diameter systolic; ESV, End-systolic volume; EDV, End-diastolic volume; FS, Fractional shortening; LVMI, Left ventricular mass index.

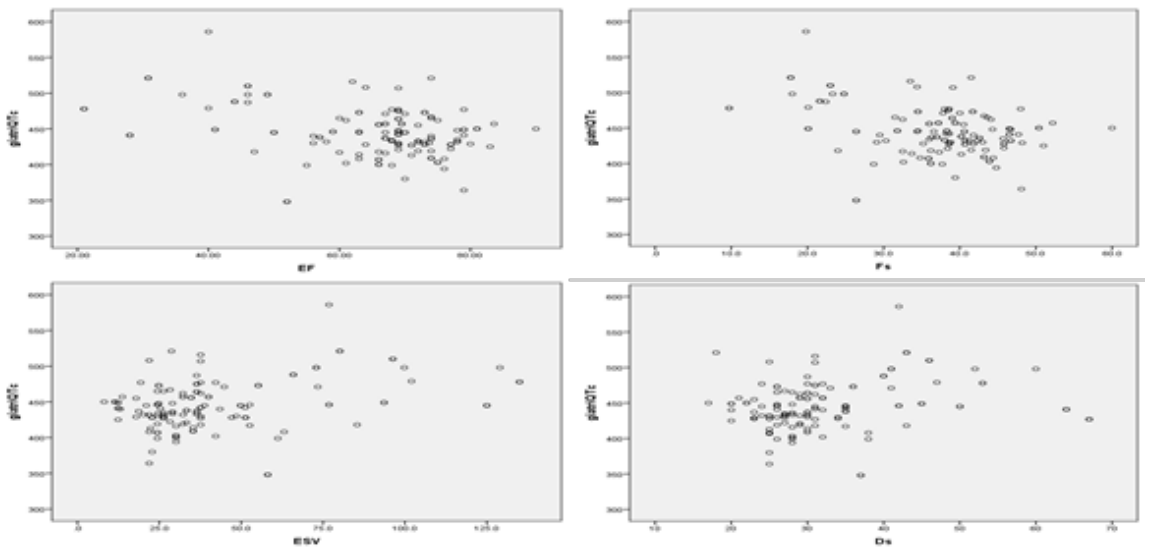

Figure 1. Correlation between QTc interval and echocardiographic parameters

From the correlation diagrams, it can be observed that there is a correlation between the QTc interval and EF, FS, ESV, and Ds (Figure 1).

4. DISCUSSION

4.1. Assessment of Prolonged QTc in Hypertensive Patients

The QT interval is measured from the onset of the Q wave to the end of the T wave on the ECG, representing the electrical systole time, which includes both the depolarization and repolarization phases of the ventricles. Numerous studies have shown that the QTc interval is influenced by several factors, including age, female gender, comorbidities, electrolyte disturbances, and various medications [7], [8]. The mechanism of prolonged QTc is related to changes in ion channels and intracellular potassium concentrations, leading to asynchronous early depolarization and repolarization. Additionally, structural changes in myocardial cells and the conduction system may also play a role in abnormal repolarization, contributing to the prolongation of the QTc interval. It is known that prolonged QTc, particularly during the repolarization phase, can lead to dangerous ventricular arrhythmias, such as torsades de pointes and ventricular fibrillation, which can be life-threatening [9].

In our study, the rate of prolonged QTc in hypertensive patients admitted to the Department of Cardiology at the University of Medicine and Pharmacy Hospital in Hue was 30.8%, with the mean QTc values in Group 1 (patients with prolonged QTc) and Group 2 (patients with normal QTc) being 489.02 ± 28.99 and 428.57 ± 20.54, respectively (Table 2). Our results showed a higher rate of 30.8% compared to the 28.3% rate found in the study by Karaye conducted on the Nigerian population in 2011 [4]. This difference may be attributed to regional and ethnic disparities. Furthermore, cardiovascular disease characteristics are often closely related to metabolism and lifestyle, meaning that the rates observed in such studies may vary depending on the time of study (2021 versus 2011).

According to a study by Guo-Zhe Sun et al. (2019), conducted on 10533 residents aged 35 and older in Liaoning Province, China, the incidence of prolonged QTc in hypertensive patients was significantly higher than in those with normal blood pressure, with similar results across all subgroups by gender and left ventricular wall thickness ($p<0.001$) [10]. Interestingly, our results were quite similar to those found in a population study conducted by Qun Ma et al. in Liaoning, China, from 2012-2013, where 31.6% of 11209 participants aged over 35 had prolonged QTc [11]. However, this rate was much lower than that found in other studies focusing on hypertensive patients. Specifically, a study by Adeseye et al. in 2012 found that 52.14% of newly diagnosed hypertensive patients in Nigeria had a maximum QTc > 440ms [12]. More recently, a 2022 study by Sathiyanarayanan et al. found that 52.5% of participants had prolonged QTc, with 59.0% in the poorly controlled hypertension group and 37.5% in the well-controlled group [13]. This is higher than the 30.8% found in our study. This

discrepancy could be explained by the smaller sample size in our study, as well as potential differences in the population and geographic location of the participants. Therefore, a larger nationwide study is necessary to accurately assess the prevalence of prolonged QTc in hypertensive patients, a chronic condition that is very common in Vietnam.

In comparison with the study by Sun et al. (2019), the mean corrected QT (QTc) values and the rate of prolonged QTc across gender, hypertension status, and left ventricular hypertrophy can be seen in the chart below [10].

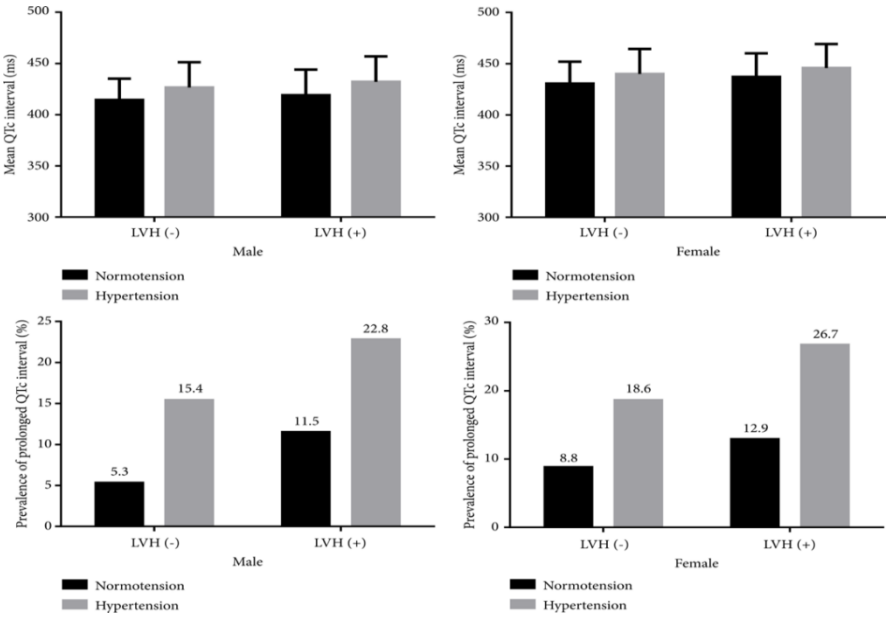

Figure 2. Mean corrected QT (QTc) values and the rate of prolonged QTc occurrence by gender, hypertension status, and left ventricular hypertrophy [10]

4.2. The Relationship and Correlation Between Prolonged QTc and Echocardiographic Parameters in Hypertensive Patients

Our study results (Table 3) show that when comparing the two groups, the mean values of left atrial diameter (LA), left ventricular ejection fraction (EF), left ventricular systolic diameter (Ds), end-systolic volume (ESV), end-diastolic volume (EDV), fractional shortening (FS), and left ventricular mass index (LVMI) showed statistically significant differences with $p<0.05$. However, there were no significant differences in the mean values of left ventricular diastolic diameter (Dd). This suggests that in hypertensive patients with prolonged QTc, there is an impact on left ventricular function.

We observed a moderate inverse correlation between QTc and EF, FS ($p<0.001$), a moderate positive correlation between QTc and ESV ($p<0.001$), and a weak positive correlation between QTc and Ds ($p=0.006$).

The study by Kang Y.J. et al. (2006) showed that left ventricular hypertrophy (LVH) affects heart function, as well as cardiovascular morbidity and mortality [14]. In our study, 92 out of 133 patients (69.17%) had left ventricular hypertrophy, which is consistent with other studies showing a statistically significant correlation between QTc and left ventricular hypertrophy in hypertensive patients. Left ventricular hypertrophy is defined as an LVMI > 95 g/m² in females and > 115 g/m² in males [15].

The results showed that in the group with left ventricular hypertrophy, EF and FS were lower in the prolonged QTc group compared to the normal QTc group, with statistical significance ($p<0.001$). However, no such difference was found in the hypertensive group without left ventricular hypertrophy (Table 4). This can be explained by the fact that left ventricular hypertrophy is a response of the heart to hypertension and LVH has significant effects on the pathophysiology of prolonged QTc [16].

Our study also noted a relationship between prolonged QTc and heart failure symptoms, such as tachycardia, edema, and dyspnea, compared to the normal QTc group, with $p<0.05$. This result is similar to the study by KM Karaye conducted on the Nigerian population [4].

5. CONCLUSION

In the study of 133 hypertensive patients, 30.8% had prolonged QTc. The QTc interval showed a

moderate inverse correlation with EF and FS, and a moderate positive correlation with ESV and Ds.

REFERENCES

1. Oikarinen L, Nieminen MS, Viitasalo M et al (2004), "QRS duration and QT interval predict mortality in hypertensive patients with left ventricular hypertrophy: the Losartan Intervention for Endpoint Reduction in Hypertension Study". *Hypertension*.; 43(5): pp.1029–34.

2. Schillaci G, Pirro M, Ronti T, et al (2006), "Prognostic impact of prolonged ventricular repolarization in hypertension". *Arch Intern Med.*; 166(8): pp.909–13.

3. Ciprian Rezuş, Victor Dan Moga, Anca Ouatu et al (2015), "QT interval variations and mortality risk: Is there any relationship?". *Anatol J Cardiol.*; 15: pp.255.

4. Karaye KM (2011), "QT interval prolongation in patients with hypertensive heart disease". *Sahel Med J.*; 13(4): pp.92–7.

5. Huynh Van Minh et al (2018), Guidelines of the Vietnam National Heart Association on diagnosis and treatment of hypertension, Vietnam Heart Association, pp.9-10.

6. Nguyen Anh Vu (2014), Updated diagnostic echocardiography, Hue University Publishing House, pp. 33-45; 190-210.

7. Robert M. Lester, Sabina Paglialunga, Ian A. Johnson (2019), "QT Assessment in Early Drug Development: The Long and the Short of It". *Int J Mol Sci.* 15; 20(1324).

8. Sami Viskin (2009), "The QT interval: Too long, too short or just right". *Heart Rhythm.*26; 6(5).pp.711-5.

9. Chhagan Lal Birda, Susheel Kumar, Ashish Bhalla et al (2018), "Prevalence and prognostic significance of prolonged QTc interval in emergency medical patients: A prospective observational study". *Int J Crit Illn Inj Sci*.; 8(1): pp.28–35.

10. Guo-Zhe Sun, Ying Zhou, Ning Ye et al (2019), "Independent Influence of Blood Pressure on QTc Interval: Results from a General Chinese Population". *Hindawi BioMed Res Int.*; pp. 1-8.

11. Qun Ma, Zhao Li, Xiaofan Guo et al (2019), "Prevalence and risk factors of prolonged corrected QT interval in general Chinese population". *BMC Cardiovasc Disord* [Internet]. 2019 Nov 29;276: pp.1-10.

12. Adeseye A. Akintunde, Adebayo T et al (2012), "QT Interval prolongation and dispersion: Epidemiology and clinical correlates in subjects with newly diagnosed systemic hypertension in Nigeria". *J Cardiovasc Res.*; 3(4): pp.290–5.

13. Sathiyanarayanan Janakiraman, Ramesh Bala Arivazhagan, Manokaran Chinnusamy. (2022), "Prevalence of QTc prolongation among hypertensive patients and its association with other co-morbidities". *Int J Adv Med.;* 9(3): pp.300-305.

14. Kang Y.J (2006), "Cardiac Hypertrophy: A Risk Factor for QT-Prolongation and Cardiac Sudden Death". *SAGE J.*; 34(1): pp.58–66.

15. Kei Mizukoshi, Masaaki Takeuchi, Yasufumi Nagata et al (2016), "Normal Values of Left Ventricular Mass Index Assessed by Transthoracic Three-Dimensional Echocardiography". *J Am Soc Echocardiogr.*; 29(1): pp.51–61.

16. Maiko Sone, Chihiro Saito, Hiroyuki Arashi et al (2021), "Association between elevated left ventricular mass index and increased cardiovascular events in patients with acute coronary syndrome: A sub-analysis of the HIJ-PROPER study". *Echocardiography*.; 39(2): pp.260–7.