Published in final edited form as:

Am J Cardiol. 2011 December 15; 108(12): 1760–1766. doi:10.1016/j.amjcard.2011.07.050.

Usefulness of Electrocardiographic QT Interval to Predict Left Ventricular Diastolic Dysfunction

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Abstract

Whether a normal electrocardiogram excludes left ventricular (LV) diastolic dysfunction (DD) and whether electrocardiographic parameters are associated with DD is unknown. We therefore sought to investigate the relation between electrocardiographic parameters and DD. We first evaluated 75 consecutive patients referred for echocardiography for clinical suspicion of heart failure (phase 1). Electrocardiography and comprehensive echocardiography were performed on all patients and were analyzed separately in a blinded fashion. Receiver operating characteristic curves and multivariate regression analyses were used to determine which electrocardiographic parameters were most closely associated with DD. Next, we prospectively validated our results in 100 consecutive, unselected patients undergoing echocardiography (phase 2). In phase 1 of our study, the mean age was 59 ± 14 years, 41% were women, 31% had coronary disease, 53% had hypertension, and 25% had diabetes. The mean ejection fraction was $54 \pm 15\%$, and 64% had DD. Of all the electrocardiographic parameters, the QTc interval was most closely associated with DD. QTc was inversely associated with E' velocity ($r = -0.54$, $p < 0.0001$), and the area under the receiver operating characteristic curve for QTc as a predictor of DD was 0.82. QTc prolongation was independently associated with reduced E' velocity ($p = 0.021$ after adjustment for age, gender, medications, QRS duration, and ejection fraction). In phase 2 of our study QTc was the electrocardiographic parameter most associated with reduced E' velocity (435 ± 31 vs 419 ± 24 ms; $p = 0.004$), confirming our phase 1 study findings. In conclusion, QTc prolongation was the electrocardiographic marker most predictive of DD and was independently associated with DD.

It is now apparent that the diagnostic and prognostic significance of left ventricular (LV) diastolic dysfunction (DD) is as important as systolic dysfunction.^{1,2} When diagnosed using comprehensive echocardiography, DD can help diagnose the heart failure (HF) syndrome and is associated with a markedly increased all-cause mortality.^{1,2} Despite the importance of diagnosing DD, there has been little study of the ability of electrocardiography to evaluate the presence or absence of DD. In addition, whether a normal electrocardiogram excludes DD is unknown. We therefore sought to evaluate whether electrocardiographic parameters can provide clues to the presence of DD. We hypothesized that the QT interval would be most closely associated with DD, given the temporal alignment of electrical repolarization and mechanical relaxation in diastole. We also hypothesized that a normal electrocardiogram would exclude a reduced ejection fraction (EF)³ but would not exclude DD on echocardiography.

Methods

Our study consisted of 2 phases. In the first phase of the study, we performed a retrospective analysis of 75 consecutive patients referred for outpatient echocardiography at the Bluhm Cardiovascular Institute (Northwestern Memorial Hospital) from January 1, 2008 to March 1, 2008. Only patients referred for echocardiography for a clinical suspicion of HF were studied. Clinical suspicion of HF was defined as any signs or symptoms of HF (e.g., dyspnea, orthopnea, lower extremity edema) that led to the ordering of an echocardiogram by the referring physician. Patients with atrial fibrillation or an irregular underlying rhythm during cardiac testing were excluded. In the second phase of the study, we prospectively validated our phase 1 findings in a convenience sample of 100 consecutive patients who were in normal sinus rhythm and who were referred for outpatient stress echocardiography from June 1, 2009 to July 15, 2009. Only the baseline echocardiograms (before exercise) were analyzed for the purposes of our study. The institutional review board at Northwestern University Feinberg School of Medicine approved both phase 1 and phase 2 study protocols. Informed consent was waived for phase 1 because the study involved only the review of existing records. All the phase 2 study participants provided written informed consent.

All subjects underwent 12-lead electrocardiography (Marquette MAC 5000 Resting ECG System, GE Healthcare, Boston, Massachusetts). In phase 2 of the study, we analyzed the baseline electrocardiographic study at rest, which was recorded with the patient in the supine position before stress testing. All electrocardiograms were analyzed by a single trained reader who was unaware of the echocardiographic findings. We documented the rhythm and measured the PR interval, QRS duration, and QT interval according to the published guidelines.^{4,5} The lead with the longest QT duration was used for the QT interval.⁴ The corrected QT interval was calculated using Bazett's formula (QTc), Fridericia's formula (QTf), and a regression-based approach developed by Sagie et al⁶ (QTs).⁴ Left atrial abnormality was defined using previously described criteria.⁷ We used the limb lead voltage or precordial lead voltage, or a combination of the 2, to define LV hypertrophy.⁸ A normal electrocardiogram was defined as: heart rate 50 to 100 beats/min, normal sinus rhythm, normal axis, PR 120 to 200 ms, QRS <120 ms, QTc <450 ms, and no abnormalities in the P-wave, QRS, ST, or T-wave morphology.

For phase 1 of the study, all subjects underwent a complete M-mode, 2-dimensional, Doppler, and tissue Doppler echocardiographic examination using a Sonos 7500 or iE33 system (Philips Medical Systems, Andover, Massachusetts) within 48 hours of their electrocardiogram. For phase 2 of the study, all patients underwent M-mode and 2-dimensional echocardiography using a Sonos 7500 or iE33 system, with additional dedicated imaging of mitral inflow using pulse wave Doppler echocardiography and pulse wave tissue Doppler echocardiography of the septal and lateral mitral annulus. For both phases of the study, 2-dimensional echocardiography, Doppler, and tissue Doppler imaging were performed according to published guidelines.^{1,9,10}

All echocardiograms were reviewed by a single trained reader who was unaware of the electrocardiographic data. The LV diastolic function was analyzed using the following indexes: mitral inflow early (E) and late (A) velocities; mitral E deceleration time; tissue Doppler early (E') and late (A') velocities of the septal and lateral mitral annulus; pulmonary venous flow characteristics; and left atrial volume. In addition, the E/E' ratio (an estimate of LV filling pressure)¹ was calculated. We graded diastolic function as follows: normal diastolic function = septal E' >8 cm/s; grade I DD = septal E' <8 cm/s and E/A ratio <0.8; grade II DD = septal E' <8 cm/s and E/A ratio 0.8 to 1.5; and grade III DD = septal E' <8 cm/s and E/A ratio >1.5 or if the E deceleration time was <150 ms. The pulmonary

venous flow characteristics and left atrial volume were used as supporting evidence for the classification of diastolic function.

For descriptive purposes, we first divided our phase 1 patients into those with normal (>8 cm/s) and abnormal (<8 cm/s) values of septal E' .¹ We then compared the demographic, clinical, electrocardiographic, and echocardiographic data between those with normal and reduced septal E' using t tests for continuous variables and chi-square (or Fisher's exact) tests for categorical variables. The p values were additionally adjusted for age, given the close association between age and tissue Doppler E' velocity. Next, we used receiver operating characteristic analysis to determine which electrocardiographic parameters were most closely associated with a decreased septal E' . We then used multivariate linear and logistic regression analyses to examine the independent association between QTc and various indexes of DD. Finally, we also examined the association between the QRS interval, JTc interval, and DD using univariate and multivariate linear regression analyses (JTc interval defined as $[QT - QRS]/RR$).

In phase 2 of the study, we again compared the clinical characteristics between those with $E' >8$ cm/s and $E' <8$ cm/s, and we analyzed the association between the QTc interval and septal E' velocity using receiver operating characteristic analyses. All statistical analyses were performed using Stata, version 10.1 (StataCorp, College Station, Texas).

Results

In the phase 1 study of 75 study consecutive patients referred for echocardiography for clinical suspicion of HF, the mean age was 59 ± 14 years, 41% were women, co-morbidities were common, and 36% had normal diastolic function, 20% had grade I DD, 29% had grade II DD, and 15% had grade III DD. The differences in the demographic and clinical characteristics between those with normal and reduced septal E' are listed in Table 1. After simple age-adjustment, β -blocker and angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use were the only clinical/demographic parameters that differed between those with normal and reduced septal E' velocity. However, several electrocardiographic and echocardiographic parameters differed between those with normal and reduced septal E' , even after age adjustment (Table 1). A prolonged QRS duration, increased QT interval, and left bundle branch block were more likely in the subjects with septal $E' <8$ cm/s.

Figure 1 displays sample tissue Doppler images and corresponding electrocardiographic tracings from 2 patients in our study, 1 with normal E' velocity and a comparison patient with abnormally reduced E' velocity. As shown in Figure 1, the patient with reduced E' velocity (signifying DD) had a greater QTc duration compared to the patient with normal E' velocity. In the entire phase 1 study sample, there was a modest, but highly statistically significant, correlation between the QTc interval and the E' velocity ($r = -0.54$, $p < 0.0001$). There was also a graded increase in the QTc interval with worsening diastolic function (Figure 2). Of all the electrocardiographic parameters (including QTf and QTs), the QTc interval was most closely associated with DD. The c-statistic (area under the receiver operating characteristic curve) for QTc as a predictor of abnormal LV diastolic function was 0.82 compared to 0.58 for electrocardiographic left atrial abnormality and 0.49 for electrocardiographic LV hypertrophy. A QTc interval of ≥ 435 ms had a sensitivity of 73% and specificity of 74% for the detection of overall DD (septal E' velocity <8 cm/s). Given the greater clinical significance of moderate or severe (grade 2 or 3) DD, we also calculated the optimal QTc interval cutpoint for more significant DD. A QTc interval of ≥ 449 ms had a 61% sensitivity and 76% specificity for the detection of more advanced (grade 2 or greater) DD. Accordingly, patients with moderate or greater DD had a more prolonged QTc

compared to patients with no or mild (grade 1) DD (QTc 461 ± 34 vs 432 ± 32 ms, respectively; $p = 0.0003$).

On multivariate analysis, QTc was independently associated with the E' velocity, E/E' ratio, and DD grade after adjusting for age, gender, β -blocker use, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use, QRS duration, and EF (Table 2). Per each standard deviation increase in the QTc interval, there was a 4-fold increase in the odds of septal $E' < 8$ cm/s (95% confidence interval 1.2 to 13.4, $p = 0.026$), and a 3.7-fold increased odds of an increased E/E' ratio > 15 (95% confidence interval 1.3 to 10.5, $p = 0.013$). Of the entire phase 1 cohort, 18 (24%) of 75 had a normal electrocardiogram. A normal electrocardiogram excluded an EF $< 50\%$. However, of the 18 subjects with normal electrocardiographic findings, 5/18 (28%) had septal $E' < 8$ cm/s (2 patients had grade 1 DD, 2 patients had grade 2 DD, and 1 patient had grade 3 DD). Therefore, a normal electrocardiogram did not exclude DD.

Because both the QTc and QRS duration were associated with DD, we performed additional analyses to determine whether the association between QTc and DD was simply due to an increased QRS duration. As stated previously, QTc was associated with DD, even after adjusting for the QRS duration. On univariate linear regression analyses, a prolonged JTc interval was associated with an increased E/E' ratio ($p = 0.005$) and worse diastolic function grade ($p = 0.041$) but not septal E' ($p = 0.077$). On multivariate linear regression analysis with JTc and QRS as independent variables and septal E' velocity as the dependent variable, we found an interaction between JTc and the QRS duration (p value for interaction = 0.014). In the 54 subjects with a normal QRS duration (< 120 ms), a significant association was found between the septal E' velocity and JTc ($p = 0.002$). However, in the 21 subjects with prolonged QRS duration (> 120 ms), JTc was not associated with reduced septal E' velocity ($p = 0.82$).

The demographic, clinical, and electrocardiographic characteristics, stratified by the normal and reduced E' velocities in phase 2 (prospective validation phase) of our study, are listed in Table 3. Overall, the phase 2 study participants (consecutive outpatients referred for stress echocardiography) were younger than the phase 1 subjects. A clinical suspicion of HF was present in 15 (15%) of 100 these subjects, and all phase 2 subjects had a normal EF ($> 50\%$). The QRS duration was prolonged in only 4 (4%) of 100 of the phase 2 subjects. DD (defined as septal $E' < 8$ cm/s) was present in 35 (35%) of the 100 subjects. Those with DD were older than those with normal diastolic function. After adjusting for age, of all the demographic, clinical, and electrocardiographic parameters, only the QTc interval differed between those with normal and reduced septal E' velocities.

The QTc duration was longer in phase 2 subjects with septal $E' < 8$ cm/s compared to those with $E' > 8$ cm/s (435 ± 31 vs 419 ± 24 ms, $p = 0.004$), confirming the association between increased QTc duration and reduced septal E' velocity. In phase 2 of the study, the c-statistic for QTc as a predictor of septal $E' < 8$ cm/s was 0.62. However, the c-statistic for QTc in the subset of phase 2 participants who had a clinical suspicion of HF was 0.87. Using a cutoff for the QTc duration > 435 ms in the unselected phase 2 out-patients undergoing stress echocardiography, the sensitivity and specificity for the detection of septal E' velocity < 8 cm/s was 43% and 77%, respectively. When restricted to patients with known or suspected HF ($n = 15$), sensitivity increased to 80% and specificity increased to 90%. Thus, QTc > 435 ms was highly specific but not sensitive for the detection of DD when studied prospectively in an unselected sample but was highly sensitive and specific when used in the subjects with suspected HF, although the sample size for the latter was small.

Discussion

In a sample of 75 consecutive patients who underwent comprehensive Doppler and tissue Doppler echocardiography for a clinical suspicion of HF, we found that although a normal electrocardiogram excludes EF <50%, it does not exclude DD. In addition, we found a linear association between a prolonged QTc duration and reduced septal E' velocity, a marker of abnormal relaxation and DD. This association persisted after adjustment for several potential confounders, including age, gender, medications, QRS duration, and EF. The association between QTc and DD was not limited to only the E' velocity, QTc was also independently associated with the E/E' ratio (a marker of LV filling pressure) and DD grade. The prospective replication of the association between the QTc interval and E' velocity in a separate group of 100 consecutive patients referred for stress echocardiography added credence to the independent inverse association between the QTc interval and E' velocity.

Ours is the first study to our knowledge to determine whether there are electrocardiographic findings that are associated with abnormal LV relaxation defined by tissue Doppler imaging. The Electrocardiographic findings that can predict DD on echocardiography are important given the diagnostic and prognostic implications of DD.^{2,11,12} Although it is now well recognized that the syndrome of HF with preserved EF is heterogeneous and can result from factors other than DD,¹³⁻¹⁵ the presence of DD helps distinguish the HF syndrome from other processes, such as pulmonary diseases resulting in dyspnea.¹⁶

A previous study of patients with hypertension and LV hypertrophy also found a modest correlation between the traditional Doppler parameters of DD (E/A ratio and isovolumic relaxation time) and QTc ($r = -0.33$ and $r = 0.35$, respectively), supporting the association between DD and QTc.¹⁷ This previous study did not include tissue Doppler imaging, which is more linearly associated with abnormal diastolic function compared to the E/A ratio and isovolumic relaxation time.¹ The use of tissue Doppler E' in our study allowed us to find a closer correlation ($r = -0.54$) between impaired relaxation (reduced E' velocity) and prolonged repolarization (QTc duration). QT prolongation has also been associated with an increased LV mass index in patients with hypertension.¹⁸ However, in our study, the QTc interval remained associated with reduced E' velocity even after adjustment for LV mass index (adjusted $p = 0.001$). Although none of the patients in our study had a diagnosis of congenital long QT syndrome, a recent study of patients with long QT syndrome found that the tissue Doppler E' was lower in patients with long QT syndrome than in healthy controls.¹⁹ Other studies have also found a link between long QT syndrome and mechanical abnormalities in cardiac contraction and relaxation.^{20,21}

The differentiation between QRS and QTc as electrocardiographic parameters associated with DD merits further discussion. We found that the JTc interval was associated with diastolic function grade and elevated E/E' ratio. However, when the E' velocity was the dependent variable, we found an interaction between QRS and JTc on multivariate linear regression analysis. JTc was more closely associated with the E' velocity in patients with normal QRS duration; however, when the QRS duration was prolonged, JTc was not associated with E' velocity. When the QRS duration is prolonged, the association between QTc and E' might be dominated by factors other than prolonged electrical repolarization (e.g., LV intraventricular and interventricular dyssynchrony) causing abnormal LV relaxation and DD. When the QRS is narrow, the association between QTc and E' appears to be a function of prolonged repolarization.

Our results should not be interpreted to indicate that the electrocardiographic QT interval can screen for or replace comprehensive echocardiography in the evaluation of patients with suspected HF or DD. Rather, our findings provide novel insight into the relation between

DD and electrical repolarization in the heart. In addition, when interpreting the results of our study, the following limitations should be considered. The initial phase of the study involved a retrospective sample that might have introduced bias into the study; however, we prospectively validated our findings in a separate group of patients. Our use of a convenience sample for validation of our findings is another potential limitation. However, despite containing different types of patients, the consistency of the findings in the 2 phases of the study support the generalizability of our conclusions that the QTc interval is the electrocardiographic parameter most associated with reduced tissue Doppler E' velocity and DD. Our study also did not include more sophisticated QT-related electrocardiographic measures such as QT dispersion. Nevertheless, the QT interval (as opposed to the QT dispersion) is an electrocardiographic parameter that is readily available and therefore more routinely applicable on a clinical basis.

Acknowledgments

This study was supported by grant 0835488N from the American Heart Association (Dallas, Texas) and an Eleanor Wood Prince grant award from the Northwestern Memorial Foundation (Chicago, Illinois) (both to S.J. Shah).

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Figure 1.

Examples of the relation between tissue Doppler E' velocity and QTc interval. Normal E' velocity and QTc interval (A) contrasted with abnormally reduced E' velocity and prolonged QTc interval (B). Asterisks denote E' wave on tissue Doppler tracings.

Figure 2.

QTc and left ventricular diastolic dysfunction grade. P-value for trend was calculated using linear regression analysis. Individual diastolic dysfunction groups were compared to normal diastolic function using *t* tests. *Asterisk* denotes $p < 0.01$ for comparison versus normal diastolic function group.

Table 1

Demographic and clinical characteristics—normal versus reduced tissue Doppler E' velocity

Characteristic	All Subjects (n = 75)	Septal E' >8 cm/s (n = 27)	Septal E' <8 cm/s (n = 48)	P-value
Age (years)	59 ± 14	52 ± 16	63 ± 10	0.0002
Women	31 (41%)	13 (48%)	19 (40%)	0.47
European American ethnicity	36 (48%)	11 (41%)	25 (52%)	0.35
African-American ethnicity	17 (23%)	3 (11%)	14 (29%)	0.09
Other ethnicity	22 (29%)	13 (48%)	9 (19%)	0.007 *
Systemic hypertension †	40 (53%)	9 (33%)	31 (65%)	0.009
Diabetes mellitus	19 (25%)	3 (11%)	16 (33%)	0.034
Coronary artery disease †	23 (31%)	4 (15%)	19 (40%)	0.02
Hyperlipidemia †	39 (52%)	11 (41%)	28 (53%)	0.14
Medications				
Diuretic	31 (41%)	6 (22%)	25 (52%)	0.01
Calcium channel blocker	10 (14%)	3 (12%)	7 (15%)	0.72
β Blocker	45 (60%)	8 (30%)	37 (77%)	<0.0001 *
Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker	44 (59%)	10 (37%)	34 (71%)	0.004 *
Statin	36 (48%)	11 (41%)	25 (52%)	0.35
Systolic blood pressure (mm Hg)	125 ± 21	124 ± 18	126 ± 21	0.81
Diastolic blood pressure (mm Hg)	74 ± 14	76 ± 13	73 ± 14	0.40
Pulse pressure (mm Hg)	51 ± 14	48 ± 13	52 ± 15	0.25
Heart rate (beats/min)	70 ± 13	70 ± 10	70 ± 15	0.95
Electrocardiographic parameters				
PR interval (ms)	164 ± 29	152 ± 24	170 ± 29	0.01
QRS interval (ms)	114 ± 34	95 ± 15	124 ± 37	0.0002 *
QT interval (ms)	417 ± 46	393 ± 24	431 ± 50	0.0004 *
QTc interval (ms)	444 ± 36	421 ± 25	458 ± 31	<0.0001 *
R-wave axis (°)	1 ± 6	25 ± 47	%13 ± 53	0.003
Left atrial abnormality	24 (32%)	6 (22%)	18 (38%)	0.17
Left ventricular hypertrophy	13 (17%)	5 (19%)	8 (17%)	0.84
Left bundle branch block	15 (20%)	0	15 (31%)	0.001 *
Right bundle branch block	4 (5%)	2 (7%)	2 (4%)	0.62
Normal electrocardiographic findings	18 (24%)	13 (48%)	5 (10%)	<0.0001 *
Echocardiographic parameters				
Left ventricular end-diastolic volume index (ml/m ²)	59 ± 25	48 ± 14	65 ± 14	0.005 *
Left ventricular end-systolic volume index (ml/m ²)	29 ± 23	20 ± 11	35 ± 26	0.004 *
Ejection fraction (%)	54 ± 15	61 ± 10	50 ± 17	0.003 *
Left ventricular mass index (g/m ²)	63 ± 24	55 ± 23	69 ± 24	0.02
Left atrial volume index (ml/m ²)	31 ± 14	25 ± 10	34 ± 14	0.008

Characteristic	All Subjects (n = 75)	Septal E' >8 cm/s (n = 27)	Septal E' <8 cm/s (n = 48)	P-value
Transmitral E velocity (cm/s)	87 ± 29	86 ± 19	88 ± 33	0.71
Transmitral A velocity (cm/s)	75 ± 24	68 ± 23	79 ± 23	0.09
E/A ratio	1.24 ± 0.59	1.31 ± 0.44	1.20 ± 0.66	0.46
E deceleration time (ms)	205 ± 57	195 ± 38	211 ± 65	0.25
Septal E' (cm/s)	7 ± 3	10 ± 2	5 ± 1	<0.0001 *
Lateral E' (cm/s)	9 ± 4	13 ± 4	7 ± 3	<0.0001 *
Septal E/E' ratio	15 ± 8	9 ± 2	19 ± 8	<0.0001 *
Lateral E/E' ratio	11 ± 6	8 ± 4	13 ± 6	<0.0001 *
Left ventricular diastolic function				<0.0001 *
Normal	27 (36%)	27 (100%)	0	
Grade 1	15 (20%)	0	15 (31%)	
Grade 2	22 (29%)	0	22 (46%)	
Grade 3	11 (15%)	0	11 (23%)	

* P-value <0.05 after adjustment for age.

[†] Systemic hypertension defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or treatment with antihypertensive drugs; coronary artery disease defined as history of abnormal stress test consistent with ischemia, documented coronary stenosis >50%, or history of percutaneous coronary intervention, coronary artery bypass grafting, or myocardial infarction; hyperlipidemia defined as history of hyperlipidemia in the medical record or treatment with cholesterol-lowering medication.

Table 2

Multivariate logistic and linear regression analyses for association of QTc interval with abnormal diastolic function *

Dependent Variable	Odds Ratio [†] (95% CI)	β -Coefficient [†] (95% CI)	P-value
E' <8 cm/s (dichotomous)	4.0 (1.2, 13.4)		0.026
E/E' >15 (dichotomous)	3.7 (1.3, 10.5)		0.013
E' (continuous) (cm/s)		-1.0 (-1.8, -0.2)	0.021
E/E' (continuous)		3.9 (1.4, 6.5)	0.003
Diastolic function grade		0.5 (0.1, 0.8)	0.010

CI = confidence interval.

* Adjusted for age, gender, β -blocker use, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker use, QRS interval, and ejection fraction.

[†] Per standard deviation increase in QTc interval.

Table 3

Demographic, clinical, and electrocardiographic characteristics in prospective validation phase of study—normal versus reduced tissue Doppler E' velocity

Characteristic	All Subjects (n = 100)	Septal E' >8 cm/s (n = 65)	Septal E' <8 cm/s (n = 35)	P-value
Age (years)	52 ± 15	45 ± 13	63 ± 9	<0.0001
Women	46 (46%)	33 (51%)	13 (37%)	0.19
European American ethnicity	57 (57%)	35 (54%)	22 (63%)	0.39
African-American ethnicity	10 (10%)	6 (9%)	4 (11%)	0.28
Other ethnicity	33 (33%)	24 (37%)	9 (26%)	0.26
Systemic hypertension	38 (38%)	21 (32%)	17 (49%)	0.11
Diabetes mellitus	6 (6%)	3 (5%)	3 (9%)	0.42
Coronary artery disease	26 (26%)	12 (18%)	14 (40%)	0.019
Hyperlipidemia	43 (43%)	23 (35%)	20 (57%)	0.036
Medications				
Diuretic	15 (15%)	8 (12%)	7 (20%)	0.30
Calcium channel blocker	13 (13%)	6 (9%)	7 (20%)	0.13
β Blocker	40 (40%)	19 (29%)	21 (60%)	0.003
Angiotensin-converting enzyme inhibitor/ angiotensin receptor blocker	34 (34%)	19 (30%)	15 (43%)	0.19
Statin	39 (39%)	18 (28%)	21 (60%)	0.002
Systolic blood pressure (mm Hg)	122 ± 18	121 ± 17	125 ± 18	0.26
Diastolic blood pressure (mm Hg)	74 ± 11	74 ± 10	74 ± 11	0.97
Pulse pressure (mm Hg)	49 ± 14	47 ± 13	51 ± 15	0.16
Heart rate (beats/min)	68 ± 15	69 ± 14	67 ± 16	0.44
Left ventricular ejection fraction (%)	59 ± 5	59 ± 5	60 ± 5	0.17
Electrocardiographic parameters				
PR interval (ms)	160 ± 27	156 ± 25	165 ± 31	0.12
QRS interval (ms)	92 ± 17	91 ± 13	96 ± 23	0.15
QT interval (ms)	404 ± 40	396 ± 35	420 ± 44	0.003
QTc interval (ms)	424 ± 28	419 ± 24	435 ± 31	0.004 *
R-wave axis (°)	34 ± 38	41 ± 39	21 ± 32	0.012

* P-value <0.05 after adjustment for age.