안정성협심증 환자에서 저명한 관상동맥 협착 유무와 좌심실 수축기능, 용적, 질량과 QT Dispersion 간의 관계

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The Relationship of the LV Systolic Function, the LV Dimension and the LV Mass to QT Dispersion in Stable Angina Patients who are with or without Significant Coronary Stenosis

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Background: The aim of this study was to investigate the relationship of the left ventricular (LV) systolic function, the LV dimension and the LV mass with the QT dispersion in patients with stable angina, and we also wanted to compare this relationship between patients with and without significant coronary stenosis on coronary angiography. ***Material and Method:*** 174 patients complained of typical angina and they had no associated ST segment or cardiac enzyme abnormalities. The patients were divided into 2 groups based on the results of coronary angiography: the patients with angiographic coronary stenosis $\geq$50% made up group I (n=101), and the patients with angiographic coronary stenosis $<$50% made up group II (n=73). An echocardiogram for assessing the LV ejection fraction (EF), the LV dimension and the LV mass and a 12-lead electrocardiogram for assessing the QT dispersion were performed before the coronary angiography. ***Result:*** The QT dispersion was significantly greater in group I than that in group II (39.8 ms vs. 33.3 ms; $p<0.05$). For all the patients, all the parameters of LV dimension and LV mass had statistically positive correlation to the QT dispersion, but the LV mass was the only independently significant parameter that was correlated with the increased QT dispersion ($p<0.05$). For group I, none of the echocardiographic parameters had significant correlation with the QT dispersion. However, the LV dimension and LV mass had significantly positive correlation with the QT dispersion, and the LV mass was also the only independently significant parameter that was correlated with increased QT dispersion in group II ($p<0.05$). ***Conclusion:*** Our study demonstrated a significantly positive correlation of the QT dispersion to the LV dimension and the LV mass in patients with stable angina. These findings are present only in patients without significant coronary stenosis.

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Key words: 1. Angina
2. Angiography
3. Stenosis

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BACKGROUND

Sudden cardiac death usually occurs due to ventricular tachyarrhythmias in patients with coronary artery disease (CAD) and left ventricular (LV) dysfunction[1]. One of the important mechanisms of arrhythmias in CAD is heterogeneity of ventricular repolarization, which may serve as a substrate for functional reentry[2]. In order to detect regional heterogeneity in action potential duration, monophasic action potential mapping can be used[3]. However, this method is invasive and cannot be performed as routine.

QT dispersion defined as the difference in duration between the longest and shortest QT interval in a 12-lead electrocardiogram was proposed by Day and associates[4] as a simple method to evaluate the heterogeneity of ventricular repolarization[5,6]. QT dispersion has been widely studied as a marker for arrhythmia risk and as a prognostic factor for some heart diseases. Increased QT dispersion has been reported in patients with a variety of heart conditions such as acute coronary syndrome[7], congestive heart failure[8], long QT syndrome[9], hypertrophic cardiomyopathy[10], malignant ventricular arrhythmias[11,12], and others. In the setting of ischemic heart disease, an increased QT dispersion has been related to the presence of myocardial ischemia[13-17] and this parameter has been defined as a predictor of viable myocardium in patients with myocardial infarction[18,19]. To my knowledge, there are no studies assessing the importance of echocardiographic LV function, dimension, and mass as a correlated parameter of increased QT dispersion in ischemic heart disease.

In this study, we attempt to investigate the relationship of LV systolic function, LV dimension, and LV mass to QT and QTc dispersion in patients with stable angina, and then to compare this relationship between patients with and without significant (≥50%) coronary stenosis on coronary angiography.

MATERIAL AND METHOD

1) Study populations

Between January 2006 and December 2006, 174 Patients underwent routine cardiac catheterization for the evaluation of typical chest pain without associated ST segment abnormalities and normal cardiac enzymes were selected for this study. Patients with acute coronary syndrome, severe valvular heart disease, chronic atrial fibrillation, decompensated congestive heart failure, conduction abnormalities, electrolyte imbalance, and antiarrhythmic drug use were excluded from this study. All patients gave written consent for the study, which was approved by the hospital committee.

2) Coronary angiography

All patients underwent coronary angiography. Coronary lesions were assessed with multiple orthogonal views and visually evaluated for morphologic features similar to those reported by the ACC/AHA. Significant coronary stenosis was defined by a 50% or more luminal diameter narrowing in one or more major coronary arteries. Patients were regarded as having without significant coronary stenosis if no significantly discrete stenosis were present. All patients were divided into 2 groups based on the result of coronary angiography: patients with angiographic coronary stenosis (≥50%), group I (n=101), and patients without angiographic coronary stenosis (<50%), group II (n=73).

3) QT measurements

A standard 12-lead ECG at a gain of 10 mm/mV and a paper speed of 25 mm/s was obtained before coronary angiography was performed. Digitally stored ECG data on the MUSE system (Marquette Medical Systems, Milwaukee, WS) was used for analysis. The QT interval was computed for all the patients by use of QT Guard software (Marquette Medical Systems, Milwaukee, WS). The QT Guard software determines T-wave compliability by means of principal component analysis. T-wave offset, T peak, and T end were computed by means of the "least square fit" algorithm and were threshold-based measurements[20]. All filters for analysis of QT dispersion were at default settings as determined by means of Marquette Medical Systems. QT dispersion was measured as the difference between the longest and shortest QT intervals in the 12-lead ECG with at least 6 measurable leads. The heart rate for each electrocardiogram was noted, and the corrected QT interval and QTc dispersion were calculated according to Bazatt's formula; $QTc=QT\sqrt{\ }/RR$.

QTc=corrected QT dispersion, RR=RR interval

4) Echocardiographic examinations

All patients underwent standard M-mode, 2-dimensional, and Doppler scanning echocardiographic examinations by university faculty using 3.0-MHz probes and an Sequior C256 Ultrasound (Acuson Inc., Mountain View, CA) prior to coronary angiography. Standard images were obtained in parasternal long and short-axis and apical four and two-chamber views with the patient in the left lateral decubitus position. For the determination of LV ejection fraction (EF) as a LV systolic function, end-systolic and end-diastolic LV volumes were measured by planimetry of the LV endocardium in the apical four-chamber view. For the determination of LV dimension, end-diastolic LV dimension, end-systolic LV dimension, thickness of interventricular septum, and thickness of LV posterior wall were measured from M-mode image in the parasternal long or short-axis view. LV mass was automatically calculated as described by Devereux and associates; LV mass (gram) = $1.04((LVDd+LVPW+IVS)^3-LVDd^3)$

LVDd=LV diastolic dimension

LVPW=thickness of LV posterior wall

IVS=thickness of interventricular septum

5) Statistical analysis

Results were presented as mean±standard deviation. QT dispersion values and other numeric variables between the 2 groups were compared by using independent t-test. Categoric variables were compared by the Chi-squared test. Pearson correlation coefficient was used in determining univariate correlation between QT dispersion and LV function, dimension, and mass in each group. Multivariate analysis for independent correlated factor to predict increased QT dispersion was evaluated by stepwise linear regression analysis. All tests were two-sided and p value <0.05 was considered statistically significant. All data were analyzed with SPSS for windows 11.0 version.

Table 1. Baseline demographic characteristics of total study population

	All patients (n=174)	Group I (n=101)	Group II (n=73)	p-value*
Age (years)	57±8	58±7	55±8	p<0.05
Sex (male %)	84 (48.3)	58 (57.4)	26 (35.6)	p<0.01
Risk factor				
Hypertension (%)	65 (37.4)	45 (44.6)	20 (27.4)	p<0.05
Diabetes (%)	45 (25.9)	31 (30.7)	14 (19.2)	p=0.114
Hyperlipidemia (%)	70 (40.2)	44 (43.6)	26 (35.6)	ns
Smoking (%)	58 (33.3)	34 (34.0)	24 (33.3)	ns
Lipid profile				
Total cholesterole (mg/dL)	196.6±49.1	200.1±56.6	191.5±35.1	ns
Triglyceride (mg/dL)	192.2±178.2	190.7±182.2	194.3±173.9	ns
HDL-cholesterole (mg/dL)	41.3±9.0	40.5±9.7	42.3±8.1	ns

*=Group I vs. Group II.

RESULT

1) Patient characteristics

The baseline demographic characteristics of the study populations are shown in Table 1. The mean age of total study population was 57±8 years and almost half of the patients were male (48.3%). The patients in group I were older ($p<0.05$) and more men and hypertension than those of group II ($p<0.01$, $p<0.05$).

2) Echocardiographic examinations

The mean EF of all patients was 65.2±8.7%. Echo examination, and LV mass in group I were significantly increased over those in group II (all $p<0.05$). Other echocardiographic parameters were statistically similar in both groups (Table 2).

Table 2. Baseline echocardiographic characteristics of total study population

	All patients (n=174)	Group I (n=101)	Group II (n=73)	p-value*
LV systolic function				
EF (%)	65.2±8.7	63.9±9.8	67.1±6.7	p<0.05
LV Dimension				
LVEDd (mm)	48.1±5.2	48.5±5.9	47.5±4.0	ns
LVEDs (mm)	29.9±5.4	30.4±6.2	29.1±3.9	ns
IVS (mm)	10.0±2.1	10.2±2.2	9.6±1.8	p=0.79
LVPW (mm)	9.8±1.6	10.1±1.6	9.5±1.5	p<0.05
LV Mass				
Mass (gram)	170.3±49.9	178.6±54.6	159.2±40.5	p<0.05

EF=Ejection fraction; LVEDd=Left ventricular end-diastolic dimension; LVEDs=Left ventricular end-systolic dimension; IVS=Interventricular septum; LVPW=Left ventricular posterior wall. *=Group I vs. Group II.

3) Automatic QT dispersion measurements

The mean baseline heart rate of all patients was 69±11, mean QT and QTc dispersion of all patients were 37.0±21.0 msec and 38.5±21.2 msec. There was no statistical difference of baseline heart rate between group I and group II. The baseline QT dispersion of group I was greater than that of group II (39.8±21.7 msec vs 33.3±19.5 msec, $p<0.05$). The baseline QTc dispersion of group I was also greater than that of group II (41.2±21.9 msec vs 34.7±19.7 msec, $p<0.05$) (Table 3).

4) Correlation of LV systolic function, LV dimension, and LV mass to QT dispersion

All patients had a significant positive correlation of QT dispersion to all parameters of LV dimension (LVDd: r=0.166, $p<0.05$; LVDs: r=0.199, $p<0.01$; IVS: r=0.153, $p<0.05$; LVPW: r=0.169, $p<0.05$) and LV mass (r=0.255, $p<0.001$), but there was no correlation between QT dispersion and LV EF. LV mass was the only significantly independent parameter on increased QT dispersion in all patients ($p<0.001$).

In group I, patients with significant coronary stenosis, LV systolic function, LV dimension, and LV mass had no significant correlation to QT dispersion. On the other hand, in group II, patients without significant coronary

Table 3. Baseline QT and QTc dispersion of total study population

	All patients (n=174)	Group I (n=101)	Group II (n=73)	p-value*
Basal heart rate (bpm)	69±11	68±12	70±10	ns
QT dispersion (msec)	37.0±21.0	39.8±21.7	33.3±19.5	p<0.05
QTc dispersion (msec)	38.5±21.2	41.2±21.9	34.7±19.7	p<0.05

QT dispersion=Longest QT interval−shortest QT interval; QTc dispersion=Longest QTc interval−shortest QTc interval. *=Group I vs. Group II.

stenosis, LV dimension and LV mass had significantly positive correlation to QT dispersion (LVDd: r=0.239, $p<0.05$; LVDs: r=0.249, $p<0.05$; IVS: r=0.322, $p<0.01$; LVPW: r=0.282, $p<0.05$; LV mass: r=0.419, $p<0.001$). However, LV mass was the only significant independent parameter on increased QT dispersion in group II, same as result of all patients (Table 4).

The relationship of LV function, LV dimension, and LV mass to QTc dispersion was statistically similar to the relationship of those to QT dispersion, except LVDd of LV dimension parameter (Table 5).

DISCUSSION

In the present study, we found three main findings. First, the QT dispersion had a significantly positive correlation with LV dimension and LV mass but not LV systolic function in patients with stable angina. Second, the QT dispersion was significantly increased in patients with significant coronary stenosis compared with those without significant coronary stenosis. Third, the correlation of LV dimension and LV mass to QT dispersion was remarkably different whether the study population has significant coronary stenosis or not. In patients without significant coronary stenosis, QT dispersion had a positive correlation with LV dimension and mass. However, any parameters had no correlation with QT dispersion in patients with significant coronary stenosis.

Changes in QT dispersion related to AMI raised the possibility that similar changes associated with transient ischemic episodes in patients with stable coronary artery

Table 4. Correlation between QT dispersion and LV function, dimension, and mass of total study population

	All patients (n=174)		Group I (n=101)		Group II (n=73)	
	r	p-value	r	p-value	r	p-value
LV systolic function						
EF	−0.105	ns	−0.062	ns	−0.119	ns
LV Dimension						
LVDd	0.166	p<0.05	0.117	ns	0.239	p<0.05
LVDs	0.199	p<0.01	0.161	ns	0.249	p<0.05
IVS	0.153	p<0.05	0.036	ns	0.322	p<0.01
LVPW	0.169	p<0.05	0.062	ns	0.282	p<0.05
LV Mass						
Mass	0.255	p<0.001*	0.142	ns	0.419	p<0.001*

EF=Ejection fraction; LVEDd=Left ventricular end-diastolic dimension; LVDs=Left ventricular end-systolic dimension; IVS=Interventricular septum; LVPW=Left ventricular posterior wall. *=Independent prognostic parameter ($p<0.05$).

Table 5. Correlation between QTc dispersion and LV function, dimension, and mass of total study population

	All patients (n=174)		Group I (n=101)		Group II (n=73)	
	r	p-value	r	p-value	r	p-value
LV systolic function						
EF	−0.124	ns	−0.081	ns	−0.142	ns
LV Dimension						
LVDd	0.129	p=0.091	0.079	ns	0.203	p=0.086
LVDs	0.188	p<0.05	0.149	ns	0.237	p<0.05
IVS	0.156	p<0.05	0.052	ns	0.301	p<0.01
LVPW	0.182	p<0.05	0.083	ns	0.281	p<0.05
LV Mass						
Mass	0.239	p<0.005*	0.133	ns	0.385	p<0.001*

EF=Ejection fraction; IVRT=Isovolumic recovery time; DT=Deceleration time; LVDd=Left ventricular end-diastolic dimension; LVDs=Left ventricular end-systolic dimension; IVS=Interventricular septum; LVPW=Left ventricular posterior wall. *=Independent prognostic parameter ($p<0.05$).

disease are of importance. This hypothesis seems particularly relevant because many instances of sudden cardiac death in this patient population may be caused by ischemia-related arrhythmia[21]. Our present study shows that QT dispersion in stable angina patients with significant coronary stenosis was statistically greater compared to those without significant coronary stenosis (average QT dispersion 39.8 msec vs. 33.3 msec, $p<0.05$). This is consistent with the finding of Roukema et al[22], Stoletniy et al[23], and Lowe et al[24], although most of their patients had multivessel disease. The important concern is that myocardial ischemia may cause heterogeneity of ventricular repolarization and can alter the regional QT interval, and thus increased QT dispersion.

Several reports showed that in patients with myocardial infarction, QT dispersion is associated with LV dilatation and deterioration of diastolic function[25-27]. Nakamae H et al suggested that QT dispersion correlates with LV systolic function rather than diastolic function in patients receiving anthracycline treatment[28]. However, our study demonstrates that LV dimension and LV mass, but not LV systolic function, have a positive correlation with QT dispersion in total study population regardless of the existence of the significant coronary stenosis. This may suggest that LV dilatation and hypertrophy are associated with increased QT dispersion in stable angina population, especially in patients without significant coronary stenosis, which is known to be associated with sudden death.

This present study shows a different pattern of correlation of LV dimension and LV mass to QT dispersion according to the existence of significant coronary stenosis. In patients without significant coronary stenosis, LV dimension and LV mass were statistically positive correlated with QT dispersion, but any parameters had no correlation with QT dispersion in those with significant coronary stenosis. Why is the different between QT dispersion and LV dimension and/or LV mass in patients with or without significant coronary stenosis? The answer to this question is not clear. Presumably, in patients without significant coronary stenosis, other factors such as LV dilatation and/or hypertrophy rather than myocardial ischemia with/without microinfarction by itself may affect QT dispersion. On the other hand, in those with significant coronary stenosis, myocardial ischemia with/without microinfarction by itself rather than environmental factors such as LV dilatation and mass may be associated with increased QT dispersion. For the further evaluation of correlation of QT dispersion to LV dimension and LV mass, in addition to LV systolic function, a randomized large study would be needed.

The present study evaluated the correlation of LV systolic function, LV dimension, and LV mass to QT dispersion in a large group of patients with stable angina. In this setting, our study demonstrates a significantly positive correlation of QT dispersion to LV dimension and LV mass in patients with stable angina. These findings are present only in stable angina patients without significant coronary stenosis. Larger studies are necessary to validate our findings.

CONCLUSION

Major limitations of the present study are the small number of patients with depressed LV systolic function in each group. Nevertheless, the fact that the study experience represents a single-center experience implies that the LV dimension and LV mass rather than LV systolic function were significantly correlated with increased QT dispersion in patients with stable angina, especially in patients without significant coronary stenosis.

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=국문 초록=

배경: 본 연구의 목적은 좌심실 수축기능, 용적, 질량과 QT dispersion간의 관계를 알아보고, 관상동맥 협착이 있는 환자와 없는 환자에서 비교하는 것이다. **대상 및 방법**: 174명의 ST분절 및 심근효소 이상소견이 없는 전형적인 안정성 협심증을 호소하는 환자들을 대상으로 하였다. Group I은 심혈관 촬영상 관상동맥 협착이 50%이상(n=101), Group II는 심혈관 촬영상 관상동맥 협착이 50%이하(n=73)인 환자로 나누었다. 심혈관 촬영 전에 좌심실 구출율, 용적, 질량을 심초음파로 측정하였고 QT dispersion측정을 위해 12-lead 심전도를 측정하였다. **결과**: QT dispersion은 Group I에서 Group II보다 유의하게 길었다(39.8 ms vs. 33.3 ms; $p<0.05$). 모든 환자에서 좌심실용적, 질량은 QT dispersion과 통계학적으로 유의한 상관관계가 있었으며, 좌심실 질량은 유일한 독립적 관계요소였다($p<0.05$). 그런데 Group I에서만 보면 초음파상에 나타난 어떤 결과도 QT dispersion과 유의한 상관관계가 없었으며, Group II에서는 좌심실 용적, 질량은 QT dispersion과 유의한 상관관계가 있었으며, 좌심실 질량은 여전히 독립적 관계 요소였다($p<0.05$). **결론**: 우리의 연구는 좌심실용적, 질량 등은 안정성 협심증환자에서 QT dispersion과 유의한 상관관계를 나타냈다. 이런 소견들은 저명한 관상동맥 협착이 없는 환자들에서만 나타난다.

중심 단어 : 1. 협심증
2. 심혈관조영술
3. 관상동맥협착