QT Variables of Isolated Mitral Valve Prolapse

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SUMMARY

Purpose: It is thought that arrhythmias are responsible for sudden deaths in patients with mitral valve prolapse (MVP). QT intervals may predict malignant arrhythmia potential in these patients. The aim of the present study is to assess QT variables in patients with MVP.

Methods: We studied 46 patients with non-rheumatic, uncomplicated and isolated MVP and 25 healthy control subjects. All individuals underwent full M-mode; two-dimensional and color-Doppler examinations. MVP was defined as superior displacement of the mitral leaflets of more than 2 mm during systole and as a maximal leaflet thickness of at least 5 mm during diastole. Maximum (QTmax), minimum (QTmin) durations, corrected QT intervals and QT dispersion were measured in every case. The results of MVP patients were compared with the data gathered from the control cases.

Results: Demographic and clinical variables were similar between the two groups. Anterior mitral leaflet thickness (AMLD), maximal leaflet displacement (DMR) and degree of mitral regurgitation (DMR) were found to be significantly higher in the patient group. QTc max, QT dispersion (QTd) and corrected QT dispersion (QTcD) were also significantly higher in MVP patients. A significant and fairly strong correlation was found between QTc max, QTcD and AMLT, MLD and DMR.

Conclusion: QT durations were significantly increased in patients with isolated MVP, which may explain increased incidence of ventricular arrhythmias and sudden death in this population. Furthermore QT variables were related with the mitral leaflet thickness and degree of mitral regurgitation; which means QT variables increases with the the severity of the disease.

Key Words: mitral valve prolapse, QT dispersion, echocardiography

Izole Mitral Kapak Prolapsusunda QT Degiskenleri

ÖZET

Amaç: Mitral Kapak prolapsusu (MKP) ile iliskili ani ölümlerden aritmilerin sorumlu oldugu düsünülmektedir. QT araligi ölçümü bu hastalardaki malign aritmi potansiyelini tahmin edebilir. Bu çalismanin amaci MKP hastalarinda QT degiskenlerini arastirmaktir.

Gereç ve Yöntem: Romatizmal ve komplike olmayan izole MKP'lu 46 hasta ve 25 saglikli birey kontrol grubu olarak çalisildi. Çalismaya alinan tüm bireylere, M-mod, 2-boyutlu ve renkli Doppler ekokardiyografi uygulandi. MKP tanimi; sistol sirasinda mitral yaprakçiklarin en az 2 mm atriuma dogru bombelesmesi ve diastolde yaprakçik kalinliginin 5 mm üzerinde saptanmasi ile kondu. Ayrica her hastada maksimum (QTmax), minimum (QTmin), düzeltilmis QT (QTc) ve QT dispersiyonu hesaplandi. MKP hastalarinin sonuçlari kontrol grubu ile karsilastirildi.

Bulgular: Hastalarin demografik ve klinik verileri kontrol grubu ile benzerdi. Hastalarin anterior mitral yaprakçik kalinligi (AMYK), maksimum yaprakçik kaymasi (MYK) ve mitral yetersizlik orani (MYO) kontrol grubundan anlamli derecede yüksekti. Yine, QTc max, QTd ve düzeltilmis QTcD hasta grubunda anlamli derecede yüksek bulundu. QTc max ve QTcD ile ekokardiyografik parametrelerden AMYK, MYK ve MYO arasinda anlamli ve oldukça güçlü korelasyon saptandi.

Sonuç: Izole MVP'li hastalarda QT araligi anlamli derecede uzamaktadir. Bu durum hasta grubunda yasanan artmis ventriküler aritmi ve ani ölüm sikligini açiklayabilir. Dahasi, QT degiskenleri mitral yaprakçigin kalinligi ve mitral yetersizlik derecesi ile, dolayisi ile MKP'nun agirligi ile iliskilidir

Anahtar Sözcükler: mitral kapak prolapsusu, QT dispersiyonu, ekokardiyografi

INTRODUCTION

Mitral valve prolapse (MVP) is one of the most common valvular heart disorders in the general population. The incidence of ventricular arrhythmias and sudden death appears to be high in this patient group (1). For instance, the incidence of premature ventricular contractions in MVP has been reported between 49 and 89% (2). The incidence is reported to increase in complicated cases such as those with an increased anterior and/or posterior leaflet thickness (=5mm), and those with severe mitral regurgitation or severe left ventricular systolic dysfunction (3). It is suggested that the underlying mechanism of the sudden death is arrhythmogenic. It was also claimed that the prolonged QT or QT dispersion intervals in MVP cases could be related to arrhythmia and sudden death (4-5). We aimed to investigate the echocardiographic and electrocardiographic features of MVP.

METHODS

The current study was carried out in the Department of Cardiology, Faculty of Medicine, Abant Izzet Baysal University between March 2000 and January 2003. Patients were recruited from those referred to our echocardiography laboratory with symptoms and/or signs consistent with a diagnosis of MVP. Patients with evidence of cardiomyopathy, congenital, or rheumatic heart disease and atrial fibrillation or conduction disturbances on resting electrocardiogram were excluded. We studied 46 patients with non-rheumatic, uncomplicated and isolated mitral anterior leaflet prolapse (14 male and 32 female with a mean age of 26.3± 5.9 years) and 25 healthy control subjects (age and sex-matched 9 male and 15 female with a mean age of 25.4 ± 4.3 years). None of the 46 subjects with mitral valve prolapse had a history of ischemic heart disease, other cardiac or systemic disease. Patients were excluded from the study if they showed evidence of inflammatory joint disease or if they had typical features of hereditary disorders of connective tissues. Other exclusion criteria were existence of hypertension, diabetes, hyperthyroidism, severe mitral regurgitation, use of drugs that can alter QT duration. All subjects have signed a written informed consent form.

Cardiological and echocardiographic assessment: All the subjects were evaluated through a complete physical examination and two independent observers performed echocardiography. All individuals underwent full M-mode; two-dimensional and color-Doppler examinations with a commercially available system (Toshiba Diagnostic Ultrasound System Model SSA 270 A, Toshiba Corporation 1992, Tochigiken, Japan) that used a 2.5 MHz. Echocardiograms were recorded with a strip chart paper recorder (Toshiba line scan recorder LSR-20B) together with lead II electrocardiogram and phonocardiogram. The measurements were carried out according to the recommendations of the American Society of Echocardiography (6). Classic MVP was defined as superior displacement of the mitral leaflets of more than 2 mm during systole and as a maximal leaflet thickness of at least 5 mm during diastole and non-classic prolapse was defined as displacement of more than 2 mm, with a maximal leaflet thickness of less 5 mm. The maximal displacement of anterior mitral leaflet was measured with both 2-D echocardiography in parasternal long-axis and apical four-chamber views and M-mode echocardiography. The anterior mitral leaflet thickness was evaluated during mid-diastole by measuring the distance from leading edge to the trailing edge of the thickness area of the mid-portion of the leaflet and thickness of rough zone of anterior mitral leaflet. Color-Doppler echocardiographic examination was used for the detection and semiquantitaton of mitral regurgitation. The degree of mitral regurgitation was assessed as the ratio of the maximal regurgitant jet area to the area of the left atrium in the parasternal and apical long axis and apical four-chamber views. Grading was performed from one of these echocardiographic windows in which the regurgitant flow was best visualized. The degree of regurgitation was considered to be trace, mild, moderate, or severe on the basis of ratios of >0% to 10%, >10% to 20%, >20% to 40%, and > 40% percent, respectively (7). Left ventricular end-diastolic dimension (LVEDD) and thickness of interventricular septum (IVST) and posterior wall (PWT) were measured at the onset of the electro-

cardiographic Q wave. Left ventricular end-systolic dimension (LVESD) was measured at time of smallest left ventricular (LV) diameter. LV fractional shortening (LVFS) was defined as (LVEDD-LVESD) X 100/LVEDD. Left ventricular end-diastolic volume (LVEDV), end-systolic volume (LVESV) and ejection fraction (LVEF) were determined from apical two or four chamber views, using the Modified Simpson method. Cardiac output (CO) was measured as the product of stroke volume and heart rate. Systemic vascular resistance (SVR) was calculated according to the formula; SVR = (mPAO-mPRA/CO) X 80, where mPRA is the mean right atrial pressure, considered equal to zero mm Hg in each subjects, and mPAO is mean aortic pressure, derived by cuff-sphygmomanometer, as diastolic blood pressure + 1/3 (systolic-diastolic blood pressure). Left ventricular myocardial weight (LVM) was calculated using the formula of Devereux et al. (8), BSA was determined from height and weight as described by Du Bois et al. (9), Left ventricular mass index (LVMI) was calculated as LVM/BSA. Systolic (AOSD) and diastolic (AODD) diameters of ascending aorta (aortic root) were measured by M-mode echocardiography in long axis view.

ECG Evaluation: ECG recordings of all subjects were done with a Schiller Writer, which records 12 derivations simultaneously at a paper speed of 50 mm/s with a calibration of 10 mV/cm. In each derivation the QT intervals were measured as the time from the beginning of the QRS to the end of the T wave in milliseconds. In the presence of a U wave, QT intervals were measured to the notch between the T and U waves. Two observers who were blinded to the clinical status of the patients carried out the QT interval measurements from each measurable derivation. Derivations with an uncertain T wave end and/or peak points, or with premature complexes, were excluded. Following the measurements, the average values were calculated. QT intervals were corrected (QTc) according to the Bazett formula. QTc prolongation was accepted as =440ms. The differences between maximum QT and QTc intervals in their own category in any of the 12 derivations were calculated as QT dispersion (QTd) and corrected QT dispersion (QTcD), respectively.

Statistical analysis: Values are presented as mean ± standard deviation (SD). Unpaired t-test was used to compare control and patients with MVP. Nonparametric ratios between groups were compared with x^2~test. Pearson or Spearmen's correlation tests were-, used to assess correlation between QT parameters and echocardiographic parameters. P value was considered significant when it is less than 0.05. "r" value was correlation efficient. The tests were performed using SPSS 7.5 for Windows.

RESULTS

Demographic, clinical and laboratory variables of control cases and the patients with MVP were shown in Table 1.

Demographic variables were not significantly different. Mean electrolyte and hematological variables were also similar between the two groups. Comparison of the echocardiographic parameters of the control cases and patients with MVP were expressed in Table 2

DISCUSSION

The results of the current study showed that mean QT durations were significantly increased in patients with isolated MVP, which may explain increased incidence of ventricular arrhythmias and sudden death in this population. Furthermore QT variables were related with the mitral leaflet thickness, degree of mitral regurgitation; which is consistent with the previous studies.

Rare cases of sudden death have been associated with MVP and it has become generally accepted that small but important subset of patients with MVP has complex arrhythmias that are potentially lethal. Both atrial and ventricular arrhythmias are common in MVP. Although the exact mechanisms have not been clarified yet, different mechanisms, such as diastolic depolarization of the muscle fibers of the anterior mitral leaflet in response to stretch, mechanical stimulation due to thickened chordae, increased excitability consequent to adrenergic system activation were speculated.

Among electrocardiographic variables QTc max, QT dispersion (QTd) and corrected QT dispersion (QTcD) were significantly higher in MVP patients (Table 3).

When electrocardiographic and echocardiographic variables were analyzed, a significant and fairly strong correlation was found between QTc max, QTcD and AMLT, MLD and DMR (Table 4).

Table 1. Demographic, clinical and laboratory characteristics of controls and the two groups of patients with MVP

	CONTROL GROUP n=25	**PATIENT GROUP n=46**
Age (years)	25.4 ±43	26.3 ± 5.9
Men/Women, n	9/16	14/32
BSA (Body surface area;m^2)	1.68±0.27	1.67±0.32
BMI (Body Mass Index :kg/m^2)	22.7 + 3.5	22.5 ± 3.7
Diastolic blood pressure (mmHg)	72.9 ±12.3	71.3 + 11.9
Systolic blood pressure (mmHg)	124.7+26.5	123.2± 21.9
Heart rate (beat /minute)	72.9 ±13.3	73.2 ± 12.7
Symptoms		
Chest pain, n (%)	1/25	23 (% 52)
Palpitations, n (%)	3/25	31 (% 71)
Dizziness, n (%)	1/25	15 (% 33)
Dyspnea n(%)	0/25	16 (% 33)
Clinical Examination		
Midsystolic click, n	0/25	33 (%71)
Systolic murmur, n	1/25	23 (%52)
Na (Meq/L)	137.5 ±7.8	138.7 ± 8.5
K (mEq/L)	4.2 ±1.5	4.3 ±1.5
Ca (mg/dl)	8.5 ±1.1	8.7 ±1.1
Mg (mg/dl)	3.4 + 0.9	3.5 ±0.8
Hb (g/dl)	13.4 ±1.1	13.0 ±1.6
Htc (%)	39.8 ± 6.5	38.3 ± 7.3

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Table 2. Conventional echocardiographic parameters, echocardiographic features of mitral leaflet in controls and patients with MVP

	CONTROL GROUP (N=25)	**MVP PATIENTS (N: 46)**	P Value
AMLT- mid-portion (mm/m^2)*	1.3±0.4	3.2+ 0.4	<0.0001
AMLT- rough zone (mm/m^2)*	1.3+0.4	3.3 + 0.5	<0.0001
MLD (mm/m^2)*	0.9 ± 0.3	2.0 ± 0.5	<0.0001
DMR (%)	8.8 ±4.3	13.9 ± 6. 5	<0.001
AODDI (mm/m^2) *	16.7+2.3	17.1 ±2.1	NS
LAD (mm/m^2)*	17.8+4.2	18.7+3.9	NS
LADV	73.8 ±7.8	78.3±8.9	NS
LASV	34.7±5.6	35.8±5.9	NS
LAEF (%)	47.3 ±5.7	45.9 ±6.3	NS
LVEDD (mm/m^2)*	27.2±3.7	28.7±4.1	NS
LVESD (mm/m^2)*.	18.5±2.1	18.8±2.9	NS
LVMI (g/m^2)	83.4+11.7	84.9+9.7	NS
LVFS (%)	33.4+6.7	35.5+5.1	NS
LVESV (ml/m^2)*	23.1±4.7	33.714.1	NS
LVEDV (ml/m^2)*	54.7±5.9	55.6±5.8	NS
LVEF (%)	62.7±8.3	63.4+6.3	NS
CO (L/m^2)*	2.23 ±0.7	2.17±0.6	NS
SVR(dyn.s.cm *)	1354±227	1337±263	NS

The abbreviations: *AMLT, anterior mitral leaflet thickness; MLD, maximal leaflet displacement; DMR, degree of mitral regurgitation; AOD diastolic diameter index of aortic wall; LAD, left atrial diameter index; LADV, left atrial diastolic volume; LASV, left atrial sytolic volume; LVEF, left atrial ejection fraction; LVEDD, left ventricular end-diastolic diameter; LVESD, left ventricular end-sytolic diameter; LVMI, left ventricular mass index; FS, left ventricular fractional shorthening; LVESV, left ventricular end-sytolic volume; LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction;* CO_t *cardiac output; SVR, systemic vascular resistance.* * These parameters were indexed by body surface area. NS: Non-significant

Table 3. Electrocardiographic parameters in controls and patients with MVP

QT parameters	Controls n=25	Patient Group n=46	P value
QT max (ms)	382 ± 25	401 ± 29	NS
QTc max (ms)	398 ± 27	429 ± 25	<0.05
QTD (ms)	33 ± 9.3	47 ± 9.7	<0.01
QT min (ms)	349 ± 21	355 ± 23	NS
QTc min (ms)	371 ± 23	374 ± 25	NS
QTc D (ms)	35 ± 9.7	54 ± 11.7	<0.001

NS: Non-significant

Table 4. The relationship between echocardiographic features of anterior mitral leaflet and QT parameters in controls and patients with MVP

	CONTROLS			MVP GROUP		
	QTC MAX	QTC MIN	QTCD	QTC MAX	QTC MIN	QTCD
AMLT (mm/m^2)	r=0.13 p>0.05	r=0.15 p>0.05	r=0.17 p>0.05	r=0.38 p<0.02	r=0.21 p>0.05	r=0.41 p<0.02
MLD (mm/m^2)	r=0.15 p>0.05	r=0.11 p>0.05	r=0.13 p>0.05	r=0.33 p<0.04	r=0.19 p>0.05	r=0.36 p<0.03
DMR (%)	r=0.09 p>0.05	r=0.08 p>0.05	r=0.11 p>0.05	r=0.35 p<0.03	r=0.17 p>0.05	r=0.40 p<0.04

The abbreviations: *AMLT; anterior mitral leaflet thickness, MLD; maximal leaflet displacement, DMR; degree of mitral regurgitation*

It is suggested that QT prolongation is related to arrhythmias in MVP cases, (10,11) but controversies still exist (12). Kulan et al. (13) reported that MVP patients who had a higher incidence of complex ventricular arrhythmias (Lown =III) had higher QTd and QTc compared with those with a lower Lown grade of arrhythmia. However, Tieleman et al. (14) did not determine such a relation. Our study confirms the results of Kulan et al (13). The main problem of this controversy is that, there are many different variables that may alter QT variables and the increase of these variables may not mean a simple "cause and effect" relation.

Previous studies have pointed out that increased QT variability reflects regional shortening as well as regional prolongation of repolarization intervals. This regional variability of the action potential interval may occur secondary to adrenergic stimulation. The increase in catecholamine levels in MVP was shown before (5). This chronically elevated plasma epinephrine may also account an increase in electrical instability which may be reflected in the ECG by a prolonged QTc.

Zouridakis et al (15), demonstrated that among the demographic and clinical variables that were tested, only the echocardiographic degree of the prolapse and anterior mitral leaflet thickness were independently associated with QT dispersion. This result is consistent with the present study.

In view of the mentioned studies, we concluded that MVP patients who had increased QT parameters should be evaluated carefully as the potential candidates of further evaluation with electrophysiological study or beta-blocker therapy, since they are more prone to sudden death.

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