doi: 10.53446/actamednicomedia.1292677

Acta Medica Nicomedia

Cilt: 6 Sayı: 2 Haziran 2023 / Vol: 6 Issue: 2 June 2023
https://dergipark.org.tr/tr/pub/actamednicomedia

Research Article | Araştırma Makalesi

EVALUATION OF CARDIAC AUTONOMIC DYSFUNCTION AND THE RISK OF ARRHYTHMIA IN CHILDREN WITH MITRAL VALVE PROLAPSE

MİTRAL KAPAK PROLAPSUSU OLAN ÇOCUKLARDA KARDİYAK OTONOMİK DİSFONKSİYONUN VE ARİTMİ RİSKİNİN DEĞERLENDİRİLMESİ

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Abstract

Objective: The occurrence of symptoms in patients with mitral valve prolapse (MVP) is linked to autonomic dysfunction and neuroendocrine causes rather than progressive mitral valve insufficiency. The goal was to assess the risk of autonomic dysfunction and arrhythmia in patients with MVP.

Methods: A cohort of 63 individuals with MVP was compared to a control group of 64 age- and gender-matched children. A comprehensive assessment was conducted, comprising physical examination, medical history taking, and various diagnostic tests, including 12-lead electrocardiography, autonomic function testing, echocardiography, and 24-hour Holter rhythm monitoring.

Results: In comparison to the control group, the MVP group had higher QTc dispersion, frontal QRS-T angle, Tp-e interval, and Tp-e/QTc ratio at rest. However, conventional measurements of heart rate variability in the Holter ECG or HRDC, a novel and understudied parameter in children, did not significantly differ between the two groups.

Conclusion: Although cases with pathological findings in the initial ECG were excluded from our study, the widened frontal QRS-T angle seen in MVP patients is a novel finding, and that when compared to the control group, these patients' HRDC doesn't seem to differ noticeably.

Keywords: Mitral valve prolapse; autonomic dysfunction; arrhythmia; child

Öz

Amaç: Mitral kapak prolapsusu (MKP) saptanan olgularda yakınmaların ortaya çıkışı ilerleyici mitral kapak yetersizliğinden çok otonomik işlev bozukluğu ve nöroendokrin nedenlere bağlıdır. Bu çalışmada MKP tanısı ile izlenen çocukların otonomik disfonksiyon ve aritmi riski açısından değerlendirilmesi amaçlanmıştır.

Yöntem: Çalışmaya primer MKP tanılı 63 hasta ve benzer yaş ve cinsiyetteki 64 çocuktan oluşan kontrol grubu dahil edildi. Tüm hastaların öyküleri alındı, fizik muayeneleri yapıldıktan sonra; 12 derivasyonlu EKG'leri, otonom işlev testleri, ekokardiyografi 24-saatlik ritim Holter incelemeleri gerçekleştirildi.

Bulgular: Ortalama dinlenme kalp hızı, hasta grubunda kontrol grubuna göre daha yüksek bulundu. Ortostatik hipotansiyon hasta grubunda 8 çocukta (%12,6), kontrol grubunda ise 4 çocukta (%6,2) saptandı. Yüzeyel EKG'de QTc dispersiyonu, frontal QRS-T açısı, Tp-e aralığı ve Tp-e/QTc oranı MKP'li hastalarda kontrol grubuna göre yüksek saptandı. Holter EKG'de kalp hızı değişkenliğini gösteren konvansiyonel ölçümler açısından iki grup arasında anlamlı fark saptanmadığı gibi HRDC açısından da iki grup arasında anlamlı fark saptanmadı.

Sonuç: Çalışmamıza başlangıç EKG'sinde patolojik bulgusu olan olgular dâhil edilmemesine rağmen MKP'li hastalarda yüksek frontal QRS-T açısının tespit edilmiş olmasının yeni ve önemli bir bulgu olduğunu düşünmekteyiz. Ayrıca yeni ve çocuklarda az çalışılmış bir parametre olan HRDC'nin MKP' li hastalarda anlamlı farklılık göstermediği ortaya çıkmış olup bununla ilgili daha fazla çalışmaya ihtiyaç vardır.

Anahtar Kelimeler: Mitral kapak prolapsusu, otonom disfonksiyon, aritmi, çocuk

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Submitted/Başvuru: 04.05.2023 • **Accepted/Kabul:** 10.06.2023 • **Published Online/ Online Yayın:** 30.06.2023

Introduction

Mitral valve prolapse (MVP) is a cardiac condition that is often asymptomatic, but may present with a range of symptoms including atypical chest pain, irregular heartbeats, shortness of breath, presyncope, reduced exercise tolerance, migraine-like headaches, severe anxiety, and depression.[1] These symptoms are thought to be caused by autonomic dysfunction, which may be due to sympathetic system dominance, neurovascular and endocrine factors, and reduced vagal tone. Palpitation and chest pain are the most commonly reported symptoms in adult patients with MVP.[2] Palpitation and chest pain were reported to be the most common complaints in an adult study.[3] Additionally, MVP may be associated with various rhythm disorders, including ventricular tachyarrhythmias, bradyarrhythmias, atrioventricular blocks, and paroxysmal supraventricular tachycardia.[4]

In patients with primary MVP, particularly in the inferior leads, nonspecific ST-T-wave changes and T-wave inversion are frequently seen. Tests used to evaluate autonomic dysfunction of the heart are orthostatic hypotension (sympathetic) and resting heart rate (parasympathetic) measurements.[5] Decreased HRV, which reflects increased sympathetic and decreased vagal activity, has been linked to ventricular arrhythmia and sudden death in the general population, particularly in those with heart disease. This study's goal was to investigate the demographics, anthropometric measures, clinical manifestations, electrocardiographic findings, rhythm Holter results, and echocardiographic findings of children with MVP, and to evaluate their risk of autonomic dysfunction and arrhythmia.

Methods

Patients

In this study, we included children aged 6 to 18 who had been diagnosed with primary MVP and were followed up with every 6 to 12 months. We also included a control group of healthy children of similar age and gender who presented to the Pediatric Cardiology Outpatient Clinic with complaints such as murmur, chest pain, syncope, or palpitation and who did not have any cardiac abnormalities identified during their evaluation. We included patients who did not attend the control during the study by contacting them by phone for an interim visit, and we also included patients who were newly diagnosed with MVP during the course of the study.

The local ethics board approved the study (Date: 26 April 2021, Number: 10/04) and all participants were informed of the study's objectives during the initial interview. We inquired about complaints such as chest pain, palpitations, dizziness, fainting, blackouts, weakness, fatigue, shortness of breath, and sweating. Body mass index was calculated by measuring height and weight. The study began with a sample of 90 MVP patients who came to the outpatient clinic control during the study, as well as patients who did not come for the control but were contacted by phone. We excluded 27 patients from the study due to drug use, additional cardiac pathology, or additional pathology that could affect ECG and rhythm Holter measurements (Figure 1).

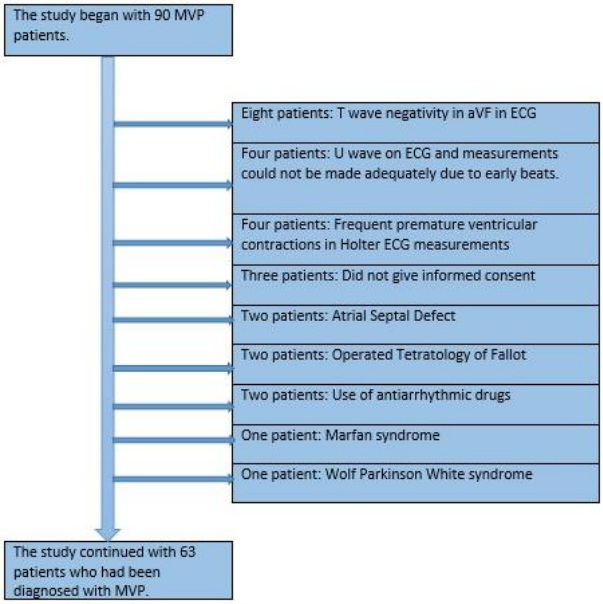

Figure 1. Flow chart of patient selection based on study inclusion criteria.

Electrocardiogram Examinations

The Cardioline ar2100view model ECG was used to record 12-lead electrocardiograms (ECGs) at a rate of 25 mm/s and an amplitude of 10 mm/mV in this study. The cases were positioned supine and given 10 minutes to rest before the ECGs were taken. The ECGs were then digitally scanned and analyzed for various parameters, including rate, rhythm, ventricular hypertrophy, atrial enlargement, QRS axis, and ST-T changes. These measurements were compared to age-appropriate normal values as reported in the literature.[6] Furthermore, QT, corrected QT (QTc), QTc dispersion, frontal QRS-T angle, Tp-e interval, and Tp-e/QTc values were investigated within the scope of the study. The study excluded leads with early beats or T waves whose end could not be determined precisely. Three QRS-T waves were assessed in each lead, and the study included cases where QT measurement could be made in at least nine leads by calculating the QT duration in milliseconds (ms).[7]

The Bazett formula was utilized to determine the corrected QT interval ($QTc = QT/\sqrt{RR}$).[8] QT dispersion was identified as the difference between the two QT intervals with the longest and shortest values recorded in the 12-lead ECG. The distance between the T wave's peak and its end in the precordial leads was identified as the Tp-e interval using the average of three different derivations. The Tp-e/QTc ratio was also calculated after Tp-e measurement. The frontal QRS-T angle was measured utilizing the difference between the QRS and T axes recorded in the ECG device's report section. For

measurements greater than 180 degrees, this angle was deducted from 360 degrees and recalculated (Figure 2).

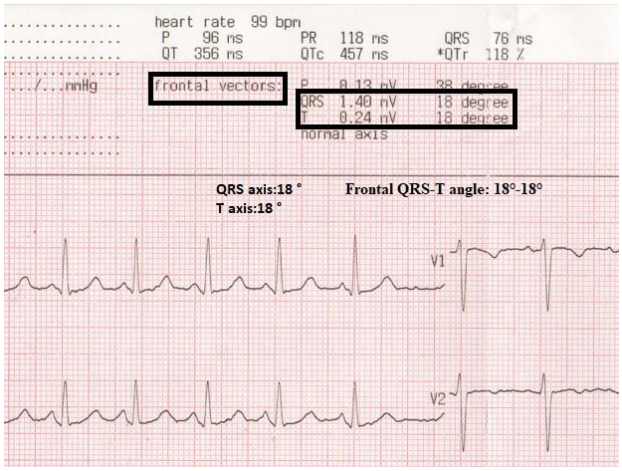

Figure2. Frontal QRS-T angle measurement on surface ECG.

Autonomic Function Tests

After a 10-minute period of rest in the supine position, the patients' ECGs, initial blood pressure measurements, and heartbeats were recorded. The participants were then instructed to stand still for 10 minutes with their arms and legs close to their bodies, and their heart rate and blood pressure were measured at the end of this time. A systolic blood pressure drop of more than 20 mmHg was considered abnormal and diagnosed as orthostatic hypotension. In this manner, orthostatic hypotension was used to assess sympathetic dysfunction and resting heart rate was utilized to assess parasympathetic dysfunction in the heart autonomic function tests.

Echocardiography

An expert cardiologist performed echocardiographic exams on study participants using a Philips Affiniti 30 model echocardiography device and an S4-2 sector probe. While the subjects were lying in the left lateral and supine positions, an echocardiographic examination was conducted using two-dimensional, M-mode, color Doppler, pulsewave Doppler, and continuous Doppler from all echocardiographic views. The diagnostic standard for MVP in the echocardiographic examination was acknowledged to be any partial or complete displacement of the anterior or posterior leaflets from the level of the mitral annulus to the left atrium greater than 2 mm.[9] The thicknesses of the anterior and posterior mitral valves were also measured. Non-classical MVP valves were defined as having a valve thickness of less than 5 mm, whereas classical MVP valves were defined as having a valve thickness of more than 5 mm.

Rhythm Holter Analysis

A 24-hour recording was taken from 38 patients with MVP and 34 subjects from the control group with a three-channel Biocare H-12 Plus model rhythm Holter device, based on the symptoms and findings (palpitation suggestive of arrhythmia, syncope, chest pain) among the subjects included in the study. Records were assessed for baseline rhythm, mean heart rate, lowest and highest heart rates, supraventricular tachycardia, premature ventricular contractions (PVC), ventricular tachycardia, supraventricular premature beat, presence of pause, and HRV. Ventricular arrhythmias detected in the patient and control groups were evaluated using the modified Lown criteria. Ventricular arrhythmias above Class 2 were considered complex ventricular arrhythmias.[10]

Time-based heart rate variability measurements are used to evaluate autonomic dysfunction, including the mean of all normal RR intervals (mean RR), standard deviation of all normal sinus RR intervals (SDNN), mean of RR intervals over all 5-minute segments in the recordings (SDANN), and consecutive normal RR intervals (mean RR). In a 24-hour rhythm Holter, automatic calculations were performed to determine the square root of the mean difference between the RR intervals (RMSSD), frequency-based heart rate variability measures such as low frequency (LF), high frequency (HF), and LF/HF ratios. Heart rate deceleration capacity (HRDC) data, which were automatically recorded on the Holter ECG device, were collected to quantitatively evaluate cardiac parasympathetic function (Figure 3).

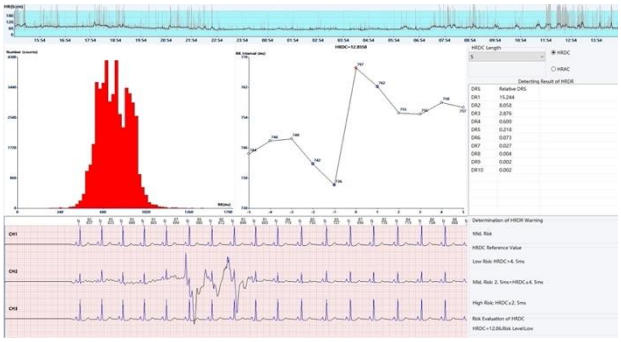

Figure3. HRDC (heart rate deceleration capacity) measurement in Rhythm Holter.

Statistical Analysis

In our study, we utilized SPSS version 26.0 as our statistical analysis program. The means and standard deviations of numerical variables were presented together. To ascertain whether the variable data were normally distributed, the Kolmogorov-Smirnov test with Lilliefors correction was used. The means were compared using the Student's t-test. The relationship between categorical data was examined using the Pearson Chi-square test. The correlation relationship was determined using the Pearson correlation coefficient. A p-value of 0.05 was considered statistically significant in each test.

Results

The study included 63 patients with primary MVP who met the inclusion criteria, as well as a control group of 64 children. Age and gender did not differ significantly between the two groups. The BMI of the patient group was discovered to be significantly lower than that of the control group ($p<0.05$) (Table 1). Nineteen (30.16%) of

the MVP patients had no symptoms. The most common symptom was chest pain, which was present in 20 (31.25%) of the children. Palpitation (20.63%), fatigue (17.46%), dispnea (12.5%), blackout (10.94%), dizziness (6.25%), syncope (6.25%), and sweating (3.13%) were the most common symptoms following chest pain. There was no discernible difference between the systolic blood pressure values at admission and control (p>0.05). The mean resting heart rate in the patient group was 97.56±16.37 beats per minute, compared to 91.61±13.56 beats per minute in the healthy group, and it was discovered to be statistically significantly higher in the patient group. (p<0.05). Orthostatic hypotension was found in 8 patients (12.6%) and 4 controls (6.2%), but the difference was not statistically significant (p=0.348).

Table 1. Demographic characteristics and body measurements of the patient and control groups

Demographic features		Patients (n=63)	Controls (n=64)	p
Sex	**Male**	43 (68.25%)	35 (54.69%)	0.165
	Female	20 (31.75%)	29 (45.31%)	
Age (years)		12.82±3.82	12.09±3.71	0.274
Body weight (kg)		41.07±13.41	44.02±14.53	0.238
Height (cm)		153.25±17.11	149.22±18.92	0.211
BMI (kg/m²)		17.03±3.07	19.12±2.76	**<0.001**

Student's t-test, BMI: Body mass index. Values were expressed as mean±standard deviation.

The ECGs of the patients with MVP and the control group were all in sinus rhythm, and the PR and QRS intervals and QRS axes were all within the normal range for their age. In either the patient or control groups, no signs of atrial or ventricular hypertrophy were detected on the ECG. While there was no significant difference in QT and QTc measurements between the patient and control groups, QTc dispersion, frontal QRS-T angle, Tp-e interval, and Tp-e/QTc ratio were significantly higher in MVP patients than in the control group (p<0.05). Furthermore, the frontal QRS-T angle was found to be greater than 90 degrees in 6 (9.3%) of the patients with MVP (Table 2).

Table 2. Electrocardiogram findings in the patient and control groups

ECG parameters	Patients (n=63)	Controls (n=64)	p
QT (ms)	353.33±23.28	352.81±22.92	0.899
QTc (ms)	391.75±26,04	396.97±21,11	0.217
QTc dispertion (ms)	25.11±10.21	21.61±8.42	**0.037**
Frontal QRS-T angle (degrees)	39.97±27.87	31.23±17.75	**0.038**
Tp-e interval (ms)	82.06±6.99	78.59±6.64	**0.005**
Tp-e/QTc ratio	0.21±0.02	0.2±0.02	**0.003**

Student's t-test. Values were expressed as mean±standard deviation.

The average amount of prolapse in MVP patients was 3.93±1.24 mm, and the average mitral valve thickness was 4.48±0.99 mm. While 4 patients (6.35%) had no mitral regurgitation (MR), 14 had trace MR, 32 had mild MR, 11 had moderate MR, and 2 had severe MR. In 47 (74.6%) patients with MVP, valve thickness was found to be less than 5 mm, and they were diagnosed with non-classical MVP. In 16 (25.3%) patients with MVP, valve thickness was found to be greater than 5 mm, and they were diagnosed with classical MVP. Though the difference between symptomatic and asymptomatic patients was not statistically significant, it was discovered that symptomatic patients had higher valve thickness and prolapse amounts. The severity of MR and the amount of MVP were found to have a strong correlation (p<0.001; r=0.76) in the correlation study, while the severity of MR and the mitral valve thickness had a positive correlation (p<0.001; r=0.48).

A 24-hour rhythm Holter monitoring was conducted in 38 (60.3%) of the MVP patients and 34 (53.1%) of the healthy peers. The mean RR, SDNN, SDANN, RMSSD, and PNN50 parameters from the time-dependent HRV measurements did not significantly differ between the patient and control groups. Furthermore, there was no discernible difference in the LF, HF, and LF/HF rates between the patient and control groups, which are frequency-based measures of heart rate variability. When HRDC measurements were compared between MVP cases and controls, no discernible difference was found (Table 3).

Table 3. Heart rate variability measurements of the patient and control groups

Heart Rate Variability	Patients (n=38)	Controls (n=34)	p
Mean RR (ms)	592.61±78.87	587.03±102.89	0.794
NN (ms)	79.02±36.72	75.48±28.44	0.648
SDANN (ms)	111±33.25	110.12±32.7	0.91
RMSSD (ms)	63.46±53.32	63.42±32.37	0.997
PNN50 (%)	16.29±14.89	13.01±12.19	0.309
HRDC	23.1±13.83	21.37±8.87	0.53
LF (ms²)	1183.91±902.53	1094.58±850.38	.665
HF (ms²)	953.91±1119.14	866.5±679.89	0.691
LF/HF ratio	1.83±1.02	1.71±1.3	0.651

Student's t-test. Values were expressed as mean±standard deviation.Mean RR: Mean of all normal RR intervals, SDNN: Standard deviation of all normal sinus RR intervals over a 24-hour period, SDANN: Standard deviation of the mean of RR intervals over all 5-minute segments, RMSSD: Root of the square of the difference between consecutive RR intervals, PNN50: 50 ms between percentage of the number of consecutive RR intervals with a difference of more than 50 ms, HRDC: Heart rate deceleration capacity, LF: Low frequency, HF: High frequency.

Discussion

There is evidence that suggests a female to male ratio of 2:1 in primary mitral valve prolapse (MVP).[11] When the demographic characteristics of the patient group were examined in our study, which included 63 patients with primary MVP and a control group of 64 healthy people, 43 (68.25%) of the patients with MVP were found to be girls and 20 (31.75%) were boys. The female/male ratio was 2.15, which was consistent with the literature. It is generally accepted that there is a relationship between asthenic body type and MVP, though this has yet to be established in children. Although this difference was not statistically meaningful, our study found that the average weight of the patient group was lower than that of the healthy controls. However, the patient group's BMI was statistically significantly lower than the healthy subjects,

which is consistent with other studies in the literature.[12,13]

Several studies have found that patients with primary MVP have a high resting heart rate due to decreased parasympathetic tone.[14,15] Catecholamine levels have also been found to be higher in patients with symptomatic MVP compared to the control group, and there is a link between autonomic dysfunction in most patients with primary MVP and regional differences in ventricular myocardium repolarization time.[16] In contrast, a study on school-age children found no significant difference in resting heart rate between MVP patients and healthy children.[17] Our study did find a statistically significant difference in mean resting heart rate between the MVP patient group (97.56±16.37/min) and the control group (91.61±13.56/min), suggesting that parasympathetic activity is suppressed in patients with MVP. Orthostatic hypotension, tachycardia, and rhythm problems are common in patients with MVP. While not statistically significant, our study found orthostatic hypotension to be more common in the MVP patient group, present in 8 children (12.6%) in the patient group and 4 children (6.2%) in the control group.

Arrhythmias are a common occurrence in individuals with mitral valve prolapse (MVP), but the majority of these arrhythmias do not pose a significant threat to the patient's well-being. In order to screen for arrhythmias, it is recommended that patients with MVP undergo routine electrocardiography (ECG), while those presenting with symptoms such as syncope and palpitations should undergo Holter ECG monitoring.[18] QT prolongation, which can be observed in MVP, has been linked to the development of ventricular arrhythmias, including ventricular fibrillation, which is a known cause of sudden death in individuals with MVP. A history of syncope with severe regurgitation, complex arrhythmias, and QT prolongation is considered a potential risk for sudden death.[13] In a study comparing healthy children to those with primary MVP, there was no significant difference in QTc intervals between the two groups. However, other research has found that the QTc intervals of patients with MVP are longer than those of healthy individuals.[7,18] In order to assess the risk of subclinical arrhythmias, our study excluded individuals with preexcitation, wide QRS complexes due to intraventricular or bundle branch block, and frequent premature atrial and/or ventricular contractions as detected by ECG or Holter monitoring. Only cases in which QT measurements were possible in at least nine leads were considered. We found that there was no significant difference in QTc measurements between the MVP and control groups. It is suggested that the differences in QTc interval results between studies may be due to variations in the methods for identifying the T wave's end.

QT dispersion, which is thought to reflect regional differences in ventricular repolarization and can serve as a marker of rhythm disturbances, has been found to be significantly higher in patients with MVP experiencing complex ventricular rhythm disorders compared to those with simple ventricular rhythm disorders in adult patients.[19,20] Similarly, pediatric patients with MVP have been found to have significantly higher QTc dispersion compared to healthy controls.[7,21] In our study, we excluded individuals with pathological findings such as frequent VEA, bundle branch block, and ST-T changes from the analysis and only evaluated subclinical cases. Despite this, we discovered that the MVP group's QTc dispersion was considerably higher than that of the healthy peers ($p<0.05$). This increase in QT dispersion in youngsters with primary MVP may be an early indicator of autonomic dysfunction of the heart, potentially preceding the detection of parasympathetic and sympathetic disorders through autonomic function testing. The QRS-T angle is a measure of myocardial repolarization that has been linked to various cardiac conditions, including ventricular hypertrophy, arrhythmias, conduction disturbances, and myocardial dysfunction. In a 2014 study, Oehler et al. found that an increased QRS-T angle was associated with left ventricular mass and a poor prognosis.[22] The frontal QRS-T angle, which has received less research attention, has been shown to triple the risk of sudden cardiac death in individuals with chronic heart disease, according to a study by Aro et al.[23] May et al. found that a widened QRS-T angle was a strong predictor of all-cause mortality and myocardial infarction in a sample of diabetic patients.[24] Our own study found that the frontal QRS-T angle was significantly higher in patients with MVP compared to controls, with 9.3% of MVP patients displaying an angle greater than 90 degrees. No study that examined the frontal QRS-T angle in a pediatric disease could be found in our literature search. The frontal QRS-T angle in children with MVP has not been studied in this manner. Patients with negative T waves in leads DI and aVF were excluded from our study because such changes could affect the T axis and result in abnormal QRS-T angles. Nonetheless, the elevated QRS-T angles observed in children with MVP suggest that it could be a useful marker for subclinical arrhythmias and sudden death.

The Tp-e interval, which represents the duration between the peak and end of the T wave on the electrocardiogram (ECG), can serve as a marker of transmural repolarization distribution. Additionally, the Tp-e/QT and Tp-e/QTc ratios can be utilized as an index of arrhythmia.[25] It has been established that prolongation of the Tp-e interval and an elevated Tp-e/QT ratio are associated with sudden cardiac death in various clinical circumstances.[26] Research has demonstrated that the Tp-e/QT ratio is a more reliable predictor of ventricular arrhythmogenesis and sudden cardiac death than the Tp-e interval.[27] In a study of adult patients with mitral valve prolapse (MVP), Yontar et al. found that the Tp-e interval, as well as the Tp-e/QT and Tp-e/QTc ratios, were significantly higher in the MVP group compared to controls.[28] Demirol et al. also observed significantly higher values for the Tp-e interval, Tp-e/QT, and Tp-e/QTc ratios in MVP patients as compared to controls in a study involving 110 MVP patients and 107 controls in children.[21] Our study discovered that the Tp-e interval and Tp-e/QTc ratio were

significantly higher in MVP patients in comparison to the control group. This differs from other studies because patients with ST-T segment changes on the ECG were excluded. We speculate that this difference is due to an increase in ventricular repolarization parameters resulting from structural changes in the mitral valve, papillary muscle, and ventricular myocardium in MVP patients, as well as increased autonomic tone.

Heart rate variability (HRV) is a measure of the fluctuation in the time interval between heartbeats. It is believed to reflect the balance between sympathetic and vagal activity in the body. Reduced HRV has been linked to an increased risk of ventricular arrhythmias and sudden death, especially in people who have heart disease. In research studies, HRV is commonly measured using time-based indices such as SDNN (standard deviation of normal-to-normal intervals), SDANN (standard deviation of the average of normal-to-normal intervals), and RMSSD (root mean square of successive differences).[29] Studies on HRV in patients with mitral valve prolapse (MVP) have produced conflicting results. Some studies have found that children with MVP have lower HRV compared to healthy controls, suggesting that the suppression of parasympathetic activity in these individuals may disrupt the balance between sympathetic and vagal activity.[30,31] On the other hand, other studies have found no significant differences in HRV between MVP patients and healthy controls.[32] In the present study, 24-hour Holter monitoring was conducted on 38 MVP patients and 34 healthy controls. Between the two groups, there were no discernible differences in the time-dependent or frequency-based HRV measurements.

Heart rate deceleration capacity (HRDC) has recently been demonstrated as a more reliable predictor of vagal tone and cardiovascular outcomes than other traditional heart rate variability (HRV) measures.[33,34] A 2018 study by Lin et al. involving 281 adult patients with end-stage renal disease found that deceleration capacity is a superior index to root mean square of the successive differences (RMSSD) in predicting left ventricular hypertrophy, regardless of kidney failure.[35] In a 2020 study on patients with Kawasaki disease, Lu et al. compared 50 patients with coronary artery involvement to 130 patients without such involvement, and found that HRDC was significantly lower in the group with coronary artery involvement, potentially making it a cardiac electrophysiological index that could be used to predict coronary artery involvement in the acute phase in children with Kawasaki.[36] In our study, there was no significant difference in HRDC measurements between cases of mitral valve prolapse (MVP) and healthy participants, although the small study population and fewer patients undergoing rhythm Holter examination may have contributed to this finding.

Limitations

Our study has several limitations, including its small sample size of 63 MVP cases, of which Holter ECG analysis was only applicable to 38. In comparison to adult population studies, our sample size is modest. Additionally, as our study was cross-sectional, we were unable to assess the patients' follow-up results.

In conclusion, our study found that MVP cases had elevated resting heart rates and more instances of orthostatic hypotension, which are key indicators of autonomic dysfunction and consistent with prior literature. We also found significant differences between healthy subjects and MVP cases in terms of QTc dispersion, frontal QRS-T angle, Tp-e interval, and Tp-e/QTc ratio, similar to the few previous studies conducted in children. The wide frontal QRS-T angle observed in MVP patients is a novel and significant finding, especially given that cases with pathological findings on initial ECG were excluded from our study. Additionally, we found that HRDC, a parameter that has only recently been studied in children with Kawasaki disease, does not differ significantly in MVP patients.

Compliance with Ethical Standards

Ethical approval was obtained from the Local Ethics Committee of Trakya University (Nisan 2021; No: 10/4).

Conflict of Interest

The authors declare no conflicts of interest.

Author Contribution

Authors contributed equally to this work.

Financial Disclosure

Financial disclosure none.

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