Original Research Article

Evaluation of Heart Rate Variability in Children with Congenital Heart Diseases Before and After Surgical Repair

Abstract

Background: Surgical repair of congenital heart diseases (CHD) affects heart rate variability (HRV) in different ways. It leads to varying degrees of cardiac autonomic derangement, clinically detectable as depression of HRV parameters. The aim of this work was to evaluate HRV in children with CHDs before and after surgical repair to detect the effect of CHDs (acyanotic or cyanotic) and cardiac surgery on cardiac autonomic function.

Methods: This observational case-control study enrolled 30 cases with CHD. Cases were divided in two equal groups: group1 included children with CHDs (not repaired) before surgical intervention and group 2 included children after surgical repair of CHDs. Another 15 healthy children, matched for age and sex, were enrolled as a control group. All children in this study were subjected to full history taking, clinical evaluation, Holter monitor, twenty-four-hour ambulatory electrocardiographic recordings and the seven time-domain indices of HRV.

Results: There was significant increase of HR in patients before surgical repair as compared to patients after surgical repair as compared to control group. There was significant decrease of PNN50, r MMSD, SDNN index and SDANN of children before surgical repair as compared to children after surgical repair as compared to controls. There was a negative significant correlation between HR and age before surgery, after surgery there was a negative significant correlation between HR and age, pNN50, rMMSD, SDNN index and SDANN, in

control there was negative significant correlation with age, SDNN index, SDANN and SDNN.

Conclusion: HRV parameters increased significantly in children with CHDs after surgical repair as compared to these before surgical repair denoting effect of cardiac surgery on cardiac autonomic function.

Keywords: Heart Rate Variability, Congenital, Heart Diseases, Surgical Repair

Introduction

Congenital heart diseases (CHDs) remain a It is the main cause of illness and death in children and the most prevalent human birth defect, affecting about one percent of all live births globally. [1]

CHDs are divided into cyanotic and acyanotic heart diseases. In general, acyanotic CHDs are more common than cyanotic group with bicuspid aortic valve disease being the most familiar kind of CHD. [2] In order to adjust for the hemodynamic changes introduced by illness, the autonomic regulation of the heart rate (HR) and of circulation might exhibit pathologic behaviour. [3]

Earlier investigations have focused on heart rate variability (HRV) in certain cardiac abnormalities like tetralogy of Fallot. The purpose of the research was to evaluate HRV in young patients diagnosed with CHDs either cyanotic or acyanotic abnormalities, comparing them to healthy control of the same age. The study's findings revealed that infants with congenital heart disease exhibit more complicated HRV and sympathetic overactivity, both of which may be an attempt to compensate for hemodynamic change.[4]

Variability in heart signal of two sequential beats is called HRV. Short and long-term variability reflect autonomic nervous system function, so that increased or decreased HRV is an indicator of human health. [5]

As a good indicator of cardiac autonomic nervous system activity, HRV has found widespread use. The various physiological elements that affect the heart's regular beat are accurately reflected in it. Actually, they are a great tool for studying the balance between the sympathetic and parasympathetic branches of the nervous system. [6]

Surgical repair of CHDs affects HRV in different ways. Depressed HRV values are a clinical marker of cardiac autonomic dysfunction. [7]

Few studies indicate that surgical aortic valve replacement may result in HRV problems. Replacement of the aortic valve surgically has a strong depressive effect on a number of cardiac autonomic measures, while less invasive techniques allow for a better presentation of HRV. [8]

Changes in cardiac autonomic regulation may influence the long-term prognosis of patients who undergo univentricular heart repair. Compared to bidirectional superior Cavo pulmonary anastomosis with antegrade pulmonary blood flow, whole Cavo pulmonary connection results in a considerable decrease in global cardiac autonomic tone. [9]

The aim of this work was to assess HRV in children with CHDs before and after surgical repair to detect the effect of CHDs (acyanotic or cyanotic) and cardiac surgery on cardiac autonomic function.

Patients and Methods:

This observational case-control study enrolled 30 children with CHDs. Cases were selected from Pediatric Cardiology Unit, pediatric Department and Cardio thoracic Surgery Department, Tanta University Hospital (TUH) between June 2018 to June 2020. The cases' parents or legal guardians provided informed consent. The Ethics Committee, Faculty of Medicine, Tanta University had approved the study.

The inclusion criteria were children in pediatric age with CHDs (acyanotic or cyanotic) before and after surgical repair. **The exclusion criteria** were hepatic diseases, renal disorders or failure, pulmonary diseases, or acute or chronic disease that can affect autonomic nervous system like diabetes mellitus.

Cases were assigned into two equal groups: group1 included children with CHDs (not repaired) before surgical intervention and group 2 included children after surgical repair of CHDs. Fifteen healthy control children, matched for age and sex, were included.

All children were subjected to the following: providing the full history including birth, personal, feeding, developmental, family history of cardiovascular events, any complaints or drug intake, diet, and physical activity. **Clinical Evaluation:** General, regional, and systemic examination as body weight, height, and vital signs such as HR, respiratory rate, and blood pressure. Cardiac examination including inspection, palpation, percussion, and auscultation for detection of cardiomegaly and evidence of murmur was performed. **Investigations:** Plain X-ray heart and chest, ECG and Echocardiography and Doppler to detect and evaluate CHDs. **Holter monitor:** Each kid in this research will undergo 24-hour Holter monitoring with ECG recording and interpretation, and heart rate variability (HRV) analysis (before and after cardiac surgery). Mathematical analysis and the assessment of HRV based on computer systems can help with the diagnosis of patient's cardiac status when coupled with 24-hour ambulatory electrocardiographic recordings and the seven time-domain (SDANN, SDNN, SDNN index, rMSSD, SD, PNN50, and mean RR) indices of HRV.

HRV parameters measured during 24 hours with Holter electrocardiogram. [10]

Calculating the 24-hour standard deviation of sinus RR intervals (SDNN). Variation in the mean normal sinus RR intervals over all 5-mm segments (SDANN). Normal sinus RR interval standard deviation across all 5-minute intervals (SDNN index). Sum of squares of the differences in RR intervals produced by regular sinus waves (rMSSD). How often the RR gap between heartbeats is more than 50 milliseconds (pNN50).

Statistical analyses

Using SPSS software, the acquired data were organised, tabulated, and statistically analysed (Statistical Package for the Social Sciences, version 21, SPSS Inc. Chicago, IL, USA). The range, mean, and standard deviation were determined for quantitative data. Boxplots were created to depict the quantitative data's median, first and third quartiles. Kruskal-Wallis ($\chi 2$ value) was computed to compare more than two means of non-parametric data, and the

Mann-Whitney U test was used to compare each pair of means if the $\chi 2$ value was significant. Pearson's correlation coefficient was used to assess the relationship between variables (r). The significance level of $p<0.05$ was selected for interpreting the findings of significance tests.

Results:

Clinical diagnosis of CHDs (before and after surgical intervention) groups. Table 1

Table 1: Clinical diagnosis of CHDs (before and after surgical intervention) groups.

Clinical diagnosis	CHD (n=30)	
	N	%
VSD	10	33.3
ASD	5	16.7
PDA	4	13.3
PFO	2	6.7
TOF	5	16.7
PA	4	13.3

VSD: Ventricular septal defect, ASD: Atrial septal defect, PDA: Patent ductus arteriosus, PFO: Patent foramen ovale, TOF: Tetralogy of Fallot, PA: Pulmonary atresia

Regarding HR of the studied children with CHDs (before and after surgical intervention) and the control group, there was a considerable increase of HR in patients before surgical repair as compared to patients after surgical repair as compared to control group. Table 2

Table 2: HR of the studied children with CHDs (before and after surgical intervention) and the control group (n=45).

HR			
Range Mean±SD	96-159 133.00±25.88	78-154 120.00±21.89	74-164 94.00±28.22
χ^2 values **P**	9.185 0.010*		
Z value **P**	G1 vs G2 & G3, P=112, 0.013* G2 vs G3, P=0.019*		

χ^2 values of Kruskal Wallis test, Z value of Mann-Whitney U test

Regarding pNN50 and rMSSD of the studied children with CHDs, there was significant decrease in children before surgical repair as compared to children after surgical repair as compared to control group. Table 3

Table 3: pNN50 and rMSSD of the studied children with CHDs (before and after surgical intervention) and the control group (n=45).

pNN50 (%)	**Children with CHDs (n=30)**		**Control children**
	Before surgical intervention	**After surgical repair**	

	(Not repaired) (n=15)	(n=15)	(n=15)
pNN50			
Range Mean±SD	0-2.80 0.74±0.93	0-17.50 1.80±5.52	0-214 38.73±63.26
χ^2 values **P**	12.773 0.002*		
rMSSD			
Range Mean±SD	1.00-32.00 13.10±9.88	3.00-61.00 16.60±16.68	10.00-88.00 52.20±27.38
χ^2 values **P**	11.996 0.002*		
Z value **P**	G1 vs G2 & G3, P=0.820*, 0.002* G2 vs G3, P=0.005*		

Regarding SDNN index, SDANN and SDNN, there was significant decrease in children before surgical repair as compared to children after surgical repair as compared to control group. Table 4

Table 4: SDNN index, SDANN, SDNN of the studied children with CHDs (before and after surgical intervention) and the control group (n=45).

	Children with CHDs (n=30)		Control children (n=15)
	Before surgical intervention (Not repaired) (n=15)	After surgical repair (n=15)	
SDNN index			
Range Mean±SD	5.00-40.00 18.10±12.02	3.00-61.00 16.60±16.68	21.00-100.00 65.90±32.21
χ^2 values **P**	13.750 0.001*		
Z value **P**	G1 vs G2 & G3, P=0.733*, 0.001* G2 vs G3, P=0.002*		
SDANN			
Range Mean±SD	14.00-38.00 25.00±10.00	0.00-87.00 31.30±24.58	34.00-159 94.20±40.16
χ^2 values **P**	15.377 0.0001*		
Z value **P**	G1 vs G2 & G3, P=0.650, 0.0001* G2 vs G3, P=0.002*		
SDNN:			
Range Mean±SD	5.00-50.00 30.20±15.60	10.00-116.00 34.50±29.71	48.00-180.00 117.60±47.81
χ^2 values **P**	17.503 0.0001*		
Z value **P**	G1 vs G2 & G3, P=0.733, 0.0001* G2 vs G3, P=0.001*		

Regarding correlation between HR and age and findings of Holer Monitor among the studied children, there was significant negative correlation between HR and age before and after surgery. pNN50, rMMSD, SDNN index and SDANN, in control there was negative significant correlation with age, SDNN index, SDANN and SDNN. Table 5

Table 5: Correlation between HR and age and findings of Holer Monitor among the studied children with CHDs (before and after surgical intervention) and the control group (n=45).

Variables	Correlation between HR and other variables among children with CHDs and control group (n=45)					
	Children with CHDs (n=30)				Control children	
	Before surgical intervention (Not repaired) (n=15)		After surgical repair (n=15)		(n=15)	
	r	P	r	P	r	P
Age	-0.716	0.020*	-0.792	0.006*	-0.725	0.018*
pNN50	-0.212	0.557	-0.678	0.031*	-0.408	0.241
rMMSD	-0.160	0.659	-0.728	0.017*	-0.630	0.051
SDNN index	-0.537	0.109	-0.860	0.001*	-0.814	0.004*
SDANN	0.510	0.1032	-0.723	0.018*	-0.720	0.019*
SDNN	0.195	0.586	-0.607	0.063	-0.766	0.006*

Discussion:

HRV is a physiological characteristic that distinguishes vegetative modulation of the heart rhythm. The relationship between a drop in HRV in patients with acute myocardial infarction (AMI) and an increase in mortality in this group of patients sparked an interest in HRV research more than four decades ago. Currently, HRV analysis is extensively researched in clinical practise to identify the effect of the parasympathetic and sympathetic systems on sinus node function, as well as the possibility of cardiovascular problems and mortality.[11]

In agreement with our study, Bakari et al. [12] studied 28 individuals with ASD between the ages of 4.5 and 8.7 years and 32 healthy control children of the same age without

hemodynamic problems underwent HRV analysis in the time and frequency ranges. All HRV measures showed to be lower in children with ASD compared to those in good health.

In a research including 39 patients who had had the Fontan operation, Butera et al. [13] found a substantial drop in HRV in the context of a reduced vagal tone. Davos et al. [14] shown that autonomic nervous system dysfunction lasted for an extended period of time after Fontan surgery. Extracorporeal circulation may also result in an imbalance of the autonomic nervous system (ANS) owing to the release of catecholamines, partial vagal denervation resulting from surgical injury, or ischemia. Massin and von Bernuth et al. [15] found reduction in HRV time and frequancy domain in CHDs cases. this decrease was connected with the functional class of heart failure as determined by the New York Heart Association, but not with any particular hemodynamic data. Massin et al. and Finley et al. [15, 16] observed HRV parameters to be considerably diminished in children with ASD. These results indicate either an increase in sympathetic heart control or a reduction in parasympathetic heart control.

In several pediatric ASD studies as mentioned by Horner and Bialkowski et al. [17, 18] the HRV values are reduced as compared with those of controls, but the values increased after defect closure.

Edwards et al. [19] observed that atrial stress is a key stimulator of atrial natriuretic peptide release. Similar to neurohumoral variables, these data indicate a potential favourable impact of lower volume and pressure on HRV. When the consequences of right atrial dilatation and tension remain for an extended length of time, ASD patients develop atrial arrhythmias.[20]

Attie et al. [21] mentioned that atrial tachyarrhythmias, thromboembolic events and heart failure are prevalent and contribute to cardiac morbidity and death in individuals..

In contrary, Hami and Corcia et al. [22] showed that there was no considerable variation regarding the HR average in children who exposed to surgery compared to controls.

Came in line with our findings, Özyılmaz et al. [23] reported significant decrease of HRV parameters of children with CHDs before surgical repair as compared to these after surgical repair. In contrary, Hami and Corcia et al. [22] showed that no considerable change was recorded concerning pNN50 in children who exposed to surgery compared to controls.

In the current study, we found that rMSSD value didn't differ in children with CHD after surgery, but it was lower in comparison to control group.

Bialkowski et al. [24] mentioned The SDNN value is more altered by parasympathetic and sympathetic impulses associated with vagal tonus than the rMSSD and pNN50 (%) values in the temporal domain study of HRV in humans.

Koca et al. [12] mentioned that Short-term HRV is represented by the HF component of frequency domain analysis and the pNN50 (%) and rMSSD values of time domain analysis (high frequency power).

Similarly, Massin and Von Bernuth et al. [25] Long-term HRV (low frequency power) is expressed by the LF component of frequency domain analysis and the SDNN, SDANN parameters of time domain analysis and SDNN index, and both are regulated by adrenergic and cholinergic activities.

In Özyılmaz et al. [23] study, The HRV values of patients who received transcatheter ASD closure at the sixth month resembled those of the control group.

In contrary, Hami and Corcia et al. [22] showed that no considerable variation was observed regarding rMSSD in children who exposed to surgery compared to controls.

Comparable to our results, Baevskii et al. [26] observed that In the sick group, the SDNN parameter was 103.0 - 50.6, compared to 138.7 - 36.2% in the controls.

In the study of Cansel et al. [27] pNN50 (percent) and rMSSD values were found to be lower in ASD patients, however this difference was not statistically significant. The HRV values in the time domain analysis rose after the procedure when compared to the initial levels, and

they neared the levels of the control group when compared to those obtained before to the surgery. One day following the surgery, the SDNN, pNN50 (%), and SDANN values rose statistically significantly. The lack of change in the rMSSD, NN, and SDNN index values may be related to the fact that the measurements were collected shortly after the surgery.

In contrary, Hami and Corcia et al. [22] showed that no considerable change was recorded concerning SDANN in children who exposed to surgery compared to controls.

In Özyılmaz et al. [23] study, ASD patients had lower rMSSD, SDNN, SDNN index, pNN50 (%) and SDANN values than the control subjects one day prior to ASD closure.

In contrary, Hami and Corcia et al. [23] showed statistically insignificant difference in SDNN in studied group compared to controls.

Literature revealed age-related variations in HRV as a result of ANS development, but occasionally contradictory findings. Some writers report a steady decline in sympathetic activity in the first decade of life[10], but others claim an increase in parasympathetic activity in the same period, as shown by elevated values of all time domain indices, followed by a gradual drop. [28]

Conclusions:

HRV parameters increased significantly in children with CHDs (acyanotic and cyanotic) after surgical repair as compared to these before surgical repair denoting effect of cardiac surgery on cardiac autonomic function.

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