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ORIGINAL ARTICLE

Echocardiographic Assessment of Ventricular Dyssynchrony in Children with Heart Failure in Zagazig University Hospitals

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ABSTRACT

Background: Cardiac failure is a significant etiology of children's morbidity and mortality. Detection of factors that may increase the severity of heart failure is very important for good management and for improving the outcome of children with heart failure. Atrio-ventricular (A.V) dyssynchrony is an important feature observed in children with heart failure and acts as a good predictor for the poor outcome of heart failure if it is not treated well. This study aimed to assess A.V dyssynchrony that may be particularly helpful for assessing the evolution and prognosis of heart failure.

Methods: This case-control study was conducted in the pediatric cardiology unit, Pediatric Department, Zagazig University Hospitals from August 2017 to April 2019. This study included 65 children divided into 2 groups. The patient group included 35 patients with heart failure in comparison to the other 30 healthy infants and children. An echocardiographic examination was performed by the same operator using a Vivid 7 computer (GE Vingmed Ultrasound, Horten, Norway) with a multi-frequency M3S and 7s transducer and an eSaote Class C machine with simultaneous ECG recording.

Results: A.V dyssynchrony is a very important prognostic measure for assessment of the severity of pediatric heart failure. Patients who died showed higher rates of A.V dyssynchrony as compared to those who survived and also showed a significant decrease in ejection fraction (EF) compared to those who did not have dyssynchrony. **Conclusions:** It was concluded that cardiac dyssynchrony is associated with an increase in the severity of heart failure and worsening of the outcome.

Key words: Echocardiographic; Heart failure; Atrio-Ventricular

INTRODUCTION

Cardiac failure is a medical or pathophysiological condition arising from ventricular dysfunction, volume or pressure overload, alone or in combination, resulting in failure of the heart to supply oxygen to satisfy the tissue's metabolic requirements [1]. The disorder is associated with a high rate of morbidity and mortality and puts a significant burden on the parents of the children affected and on society, making it one of the most severe and serious childhood conditions [2].

Atrio-ventricular (A.V)dyssynchrony refers to the abnormal prolongation of the timing of contraction or relaxation between the atrium and the ventricle [3]. Echocardiographic assessment of cardiac dyssynchrony has been extensively used because it is noninvasive, widely available, and has no known risk or side effect. Most of the assessment modalities used are tissue doppler imaging. However, more recent studies have employed the use of speckle-tracking echocardiography and 3-dimensional echocardiography [4]. This study aimed at assessing the ventricular function and

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A.V dyssynchrony by the different echocardiographic modalities, including tissue Doppler imaging and deformation imaging (strain and stain rate), as well as by ECG in children with heart failure.

METHODS

Patients and study design

The study was carried out from August 2017 to April 2019 at the Pediatric Cardiology Unit, Pediatric Department, Zagazig University Hospitals. This is a case-control study that included 65 children divided into 2 groups: the patient group that included 35 patients with heart failure in comparison to the control group that included 30 healthy infants and children. Age and sex were matched in both groups.

Inclusion criteria: all pediatric cases who were diagnosed to have heart failure and ventricular dysfunction, either due to congenital heart diseases (CHD), cardiomyopathy or myocarditis were involved in our study from both sexes with age more than one month and less than 15 years. Control children with matched age and gender to the cases who attended the outpatient clinics at the Pediatric Hospital of Zagazig University. Both had no significant history of cardiac or systemic disorders and had normal results in clinical, electrocardiographic, and echocardiographic testing. Exclusion criteria: children with congenital anomalies as chest or gastrointestinal anomalies, children aged less than one month or more than 15 years and children who have undergone any cardiac surgery were excluded from the study. Also, children with single ventricle anomalies were excluded.

Echocardiography:

Echocardiographic exams were performed with all subjects positioned in the supine decubitus and left lateral decubitus with sedation if required using oral chloral hydrate.

Echocardiographic exams were performed by the same operator using a Vivid 7 computer (GE Vingmed Ultrasound, Horten, Norway) with multi-frequency M3S and 7s transducer and an eSaote Class C machine with simultaneous ECG recording at The Echocardiography Laboratory of Children's Hospital, Zagazig University.

Routine diagnostic imaging, including mapping of color stream, pulsed, and continuous wave doppler, was initially performed. Color doppler myocardial imaging with regular subcostal, four-chamber apical, short axis, and long parasternal and suprasternal views.

To achieve a frame rate of 130 ±20, sector size and depth were chosen. To maximize color saturation, gain levels, filters, and pulse repetition frequencies were modified, and continuous electrocardiographic monitoring was used throughout the test.

During normal quiet breathing, three consecutive cardiac cycles were captured. Data has been registered. The studies were recorded on video for further evaluation.

1-Cardiac Dimensions:

Echocardiographic tests were conducted as prescribed by the American Echocardiography Society [5]. Aortic (AO) and left atrial (LA) dimensions, from the parasternal short axis view, the central pulmonary artery, right and left pulmonary branches are calculated. Interventricular septum (IVS), left ventricular rear wall thickness (LVPW), left ventricular end diastolic (LVED) and left ventricular end systolic (LVES) measurements are determined from the parasternal long axis view with sound plane orientation just below the mitral valve tips. The right ventricular end-diastolic diameter (RVEDD) was measured in millimeters (mm) and corrected for body surface area measured from the parasternal short axis view.

2- Systematic echocardiographic assessment:

Evaluation of cardiac valves' function and morphology: from the apical 4-chamber and the long parasternal axis views, the mitral and tricuspid valves are studied. From the apical 5-chamber and the long parasternal axis views, an aortic valve was studied. From the parasternal

short axis view, the pulmonary valve was evaluated at the level of the broad arteries.
Evaluation of cardiac septa: interatrial septum was visualized from the subcostal sagittal view. Interventricular septum was examined from the apical 4-chamber, apical 5-chamber, long parasternal axis, and short parasternal views.
Evaluation of wall motion abnormalities: anomalies in the septal and left ventricular wall movement are analyzed from the long parasternal axis, the short parasternal axis, and the apical four chamber views. Detailed examination and description of the underlying CHD.
3- Conventional ventricular functions:
Conventional LV systolic functions: M-mode images were used to calculate the LVED and LVES [6] (Figure 1).
4-Evaluation of Dyssynchrony
Evaluation of the relationship between heart rate and measures of dyssynchrony
Evaluation of the relationship between each dyssynchrony measure and age was determined using both raw data and data corrected for heart rate according to Bazett's formula [7]:

Dyssynchrony corrected= (Dyssynchrony uncorrected)/√(2&RR)

Where "Dyssynchrony corrected" is the final corrected value in milliseconds for each dyssynchrony measure of a given child in cases or commands, "dyssynchrony corrected" is the dyssynchrony measure of interest in milliseconds derived from that individual child, and "RR" is the period in seconds between two consecutive R electrocardiogram waves [8]. Cardiac dyssynchrony was assessed by the following criteria:
1-Assessment of atrioventricular dyssynchrony:
Atrioventricular synchrony is established when the diastolic atrioventricular inflow waves of early (E) and late (A) are distinct and the ventricular contraction of the A-wave is not prematurely terminated. Dyssynchrony takes place at an extended A-V interval and if the end of the A-wave is not associated with the complex QRS and/or mitral valve press (Figure 2).
2-Assessment of interventricular dyssynchrony:
Interventricular mechanical delay (IVMD) using the pulsed doppler mode, defined as the difference between the aortic and pulmonary pre-ejection delay (abnormal if ≥40 ms), it is the time from the onset of the QRS complex to the beginning of each respective systolic contraction, measured for both right and left ventricular outflows.
3-Assessment of intraventricular dyssynchrony:
Septal to posterior wall motion delay (SPWMD) using M-mode imaging (abnormal if ≥130 ms). The septal to posterior wall delay can be measured by M mode. By calculation of time difference between peak displacement of the basal septal and posterior wall segments. In short axis parasternal view at level of papillary muscle.
Ethical Clearance: Written informed consent was obtained from the patients' parents to participate in the study. Approval for performing the study was obtained from Pediatrics Department, Zagazig University Hospitals after taking Institutional Review Board (IRB) approval. The work has been carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Statistical analysis

Data was collected, coded, updated, and entered into version 20 of the Social Science Statistical Suite (IBM SPSS). Statistics were provided as quantitative statistics numbers and percentages, mean, standard deviations (SD), and quantitative data ranges with parametric distribution and inter-quartile median (IQR) for non-parametric distribution of quantitative data. The chi-square test compared qualitative data of the two groups. The exact Fisher test was used instead of the chi-square test when the predicted count was found in any cell below 5.
Specific t-tests were used to compare two groups with quantitative data and a parametric

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distribution, and Mann-Whitney tests were used to compare two groups with quantitative data and a non-parametric distribution.

The confidence interval was set at 95% and the agreed margin of error was set at 5%. The p-value was therefore considered significant as the following:

P > 0.05= non-significant, P < 0.05=significant, P < 0.01=highly significant.

RESULTS

Table 1 shows that there was a highly statistically significant increase of the echocardiographic dimensions in the patients' group in comparison to the control group. Table 2 shows that there was a highly statistically significant decrease in tissue Doppler in the patients' group in comparison to the control group. Table 3 showed that 51.4% of patients had A.V dyssynchrony. Table 4 shows that patients who died had a statistically significant higher rates of A.V dyssynchrony as compared to those who survived. Table 5 shows that the patients who had A.V dyssynchrony showed significant decrease in the EF compared to those who did not have.

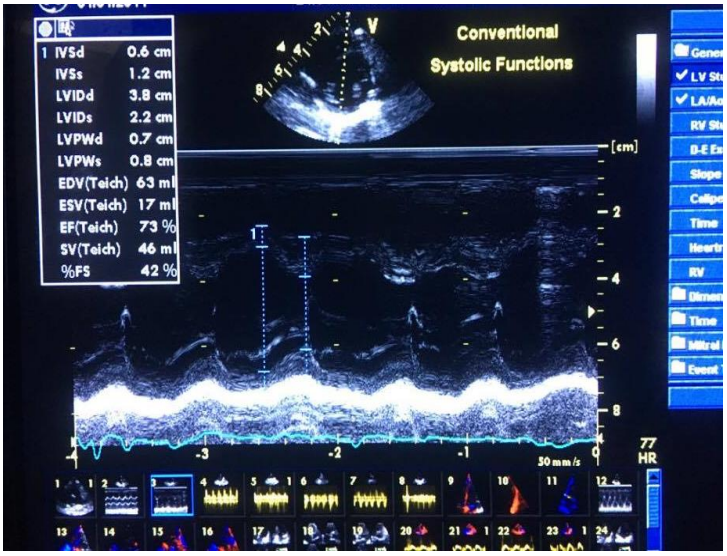

Figure 1: Conventional LV systolic functions

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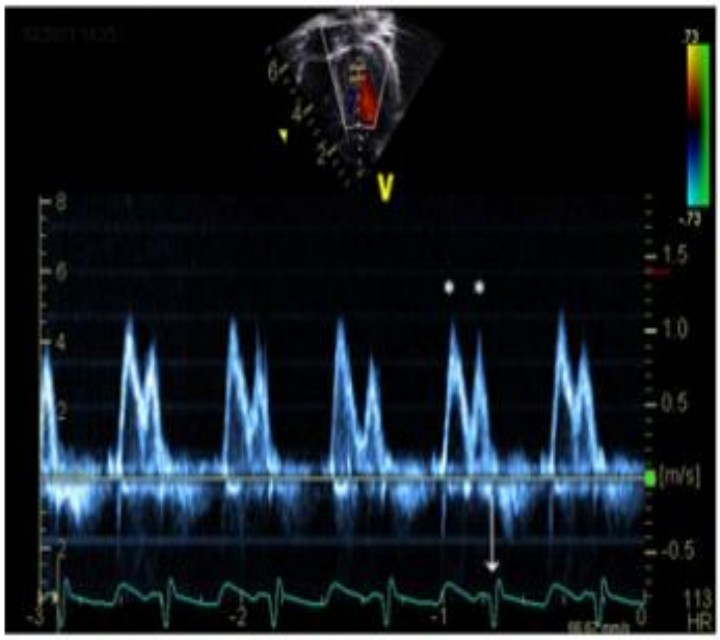

Figure 2: Atrio-ventricular dyssynchrony by mitral inflow doppler. Atrioventricular synchrony is optimal when distinct E and A waves are seen (asterisks) and the A wave terminates concurrent with the QRS complex (arrow) and not prematurely due to ventricular contraction.

Table 1: Echocardiographic dimensions in the patients' and control groups

Dimensions	Control group (Number=30)		Patient group (Number=35)		Independent t-test	
	Mean	SD	Mean	SD	t	P value
IVSD	6.23	1.35	8.77	2.51	-4.946	0.001 **
LVPWD	5.64	1.39	9.33	3.67	-5.197	0.001 **
LVED	26.18	3.92	40.81	10.67	-7.105	0.001 **
LVES	14.06	2.74	29.50	10.70	-7.681	0.001 **
R.V	19.66	2.78	34.87	11.23	-7.223	0.001 **

*significant **highly significant
IVSD =Interventricular Septum Diastolic Dimension
LVPWD =Left Ventricular Posterior Wall
LVED =Left Ventricular End Diastolic Dimension
LVES =Left Ventricular End Systolic Dimension
R.V=Right ventricle

Table 2: Echocardiographic findings in the patient and control groups regarding tissue Doppler

Tissue Doppler		Control group (Number=30)		Patient group (Number=35)		Independent t-test	
		Mean	SD	Mean	SD	t	P-value
Lateral Mitral	**S'**	0.07	0.01	0.05	0.01	8.236	<0.001 **
	E'	0.13	0.02	0.09	0.04	6.064	<0.001 **
	A'	0.07	0.01	0.07	0.03	0.150	0.881

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Tissue Doppler		Control group (Number=30)		Patient group (Number=35)		Independent t-test	
		Mean	SD	Mean	SD	t	P-value
Medial Mitral	**S'**	0.08	0.01	0.05	0.01	7.852	<0.001 **
	E'	0.12	0.01	0.08	0.03	6.780	<0.001 **
	A'	0.07	0.01	0.07	0.03	0.590	0.558
Lateral Tricuspid	**S'**	0.09	0.01	0.07	0.02	4.301	<0.001 **
	E'	0.14	0.02	0.11	0.03	4.710	<0.001 **
	A'	0.10	0.02	0.08	0.03	3.084	0.003 **
Medial Tricuspid	**S'**	0.08	0.01	0.05	0.02	7.146	<0.001 **
	E'	0.13	0.01	0.09	0.04	5.954	<0.001 **
	A'	0.07	0.01	0.07	0.03	0.044	0.965

*significant **highly significant
S' =Systolic Tissue Velocity
E'=Early Diastolic Tissue Velocity
A'=Late Diastolic Tissue Velocity

Table 3: Frequency of atrioventricular dyssynchrony in patient groups

Dyssynchrony	Patient group (Number=35)	
	Number	Percentage
Atrio-Ventricular dyssynchrony	18	51.4

Table 4: Relation between atrioventricular dyssynchrony and the outcome

Dyssynchrony		Outcome of disease				Chi-square test	
		Death		Survival		X^2	P-value
		Number	%	Number	%		
A.V dyssynchrony	**Negative**	0	0.0%	17	54.8%	4.265	0.038 *
	Positive	4	100.0%	14	45.2%		

***significant** ****highly significant**

Table 5: Relation between atrioventricular dyssynchrony and EF

Dyssynchrony		E.F		Independent t- test	
		Mean	SD	t	P-value
A.V dyssynchrony	**Positive**	49.77	13.46	-2.159	0.038 *
	Negative	52.23	14.07		

*:significant **:highly significant
A.V Dyssynchrony= atrioventricular dyssynchrony
E.F =ejection fraction

DISCUSSION

Pediatric heart failure is a very important cause of morbidity and mortality in children. heart failure related cardiovascular disorders affect myocardial functions, primarily due to systemic or diastolic dysfunction. Atrio-ventricular dyssynchrony is a very serious feature observed in children with heart failure [9]. Cardiac dyssynchrony is uncoordinated contractions of different segments of the heart, which is classified as atrioventricular, interventricular, and intraventricular dyssynchrony [10]. Atrioventricular dyssynchrony is caused by dysfunction of the sinus and atrioventricular node, causing a lag between atrial and ventricular contraction [11].

Interventricular dyssynchrony occurs due to discordance between right and left ventricular contractions as in cases with BBB. Intraventricular dyssynchrony results in

unequal and ineffective contraction of the ventricular myocardium because of areas of early and late activation. This contributes to altered ventricular performance, resulting in inefficient myocardial mechanics and impairment of the ventricular ejection [11].

The well-established echocardiographic methods to assess cardiac dyssynchrony include M-mode echocardiography, tissue Doppler imaging, routine pulsed doppler imaging, speckle-tracking imaging, cardiac magnetic resonance imaging, and three-dimensional echocardiography [3].

In this study, we found a statistically significant increase in the patient group compared to the control group regarding echocardiographic dimensions. This is in agreement with Gowda et al. [12], who stated that the heart failure group had larger LV diastolic, and LV systolic dimensions compared to their controls.

Among various echocardiographic techniques, tissue Doppler imaging has gained acceptance due to its ability to define regional timing and contractility, and high reproducibility [13]. Regarding dyssynchrony, it was revealed that 62.9% of patients had A.V dyssynchrony. This study revealed that children who had A.V dyssynchrony showed a decrease in the EF, and this is in accordance with Zhou et al. [14] and Gowda et al. [12], who found that cases with systolic dyssynchrony showed a decrease in the EF. There are few studies in pediatric heart failure patients that identified systolic dyssynchrony. Friedberg et al. [15] were the first to evaluate ventricular dyssynchrony using tissue Doppler imaging and velocity vector imaging in pediatric heart failure patients with a negative correlation between dyssynchrony and cardiac function.

Patients who died showed statistically significant higher rates of atrio-ventricular dyssynchrony compared to those who survived. In our research, there was a statistically significant increase in hospitalization in dyssynchronized patients.This is in accordance with Fauchier et al. [16], Bader et al. [17], and Penicka et al. [18], who confirmed that cardiac dyssynchrony is a prognostic indicator of cardiac endpoints.

Therefore, echocardiographic measures of dyssynchrony play a primary role in patient selection for potential treatment with CRT and also in evaluating its utility in predicting the response to CRT in children and adolescents with advanced heart failure [13].

The present study has some limitations, including a small number of patients and that we included children with heart failure mainly depending on clinical and echocardiographic diagnosis, so further studies with a larger number are required.

CONCLUSIONS

According to the results of our study, we concluded that cardiac dyssynchrony is an important phenomenon occurring in children with heart failure and associated with deterioration of the outcome.

RECOMMENDATIONS

Echocardiographic evaluation should be done to pediatric patients with heart failure on admission and ventricular dyssynchrony must be taken in consideration during evaluation of heart failure so further studies on larger number of pediatric patients is recommended to explore the value of investigating cardiac dyssynchrony in children with heart failure and comparison between the different methods of dyssynchrony assessment. So future studies are needed to evaluate the potential use of resynchronization therapy in pediatric heart failure tailored according to the dyssynchrony study results.

Conflict of interest

The authors report no conflicts of interest. The authors along are responsible for the content and writing of the paper.

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