

Assessment of Atrial Electromechanical Delay Using Tissue Doppler Echocardiography in Children with Bronchial Asthma

Somaia A. Elwan^a, Ahmed A. Mohamed^b, Alaa E. Elsayad^a, Eman G. Abdelrahman^a

^aPediatrics Department, Faculty of Medicine Benha University, Egypt.

^bChest diseases Department, Faculty of Medicine Benha University, Egypt.

Corresponding to: Alaa E. Elsayad, Pediatrics Department, Faculty of Medicine, Benha University, Egypt.

Email:
alaa2018elsayad@gmail.com

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Abstract

Background: Electrocardiographic abnormalities are common in asthma. Atrial electromechanical delay (AED) assesses the atrial conduction properties and was used to predict risks of arrhythmias in bronchial asthma using tissue doppler echocardiography. **The aim** of this work was to assess AED using tissue doppler echocardiography in children with asthma.

Methods: This case control study was carried out on 40 asthmatic children aged from 8 to 16 years, both sexes, diagnosed with asthma, suggested by recurrent symptoms of cough, chest tightness, difficult breathing and wheezing responding to bronchodilators (patients' group) and 40 healthy children (control group). History, physical examination, conventional echocardiographic and tissue doppler assessment including atrial electromechanical delay and myocardial performance index (MPI) were performed for both groups.

Results: The dimensions of the right atrium (RA), P-wave dispersion (PWD), isovolumic contraction time (ICT), isovolumic relaxation time (IRT), ET (ejection time), MPI, right ventricular (RV), intra-right atrial conduction time (IRCT) and inter-atrial conduction time (IACT) were significantly higher in the asthmatic group ($p < 0.05$). IRCT and IACT were significantly higher in the asthmatic group. There were significant positive correlations between IRCT and age, severity of asthma, duration of illness, ICT and IRT while a significant negative correlation between IRCT and the peak expiratory flow rate (PEFR). There were significant positive correlations between IACT and Tricuspid S (Annular peak velocity during systole) and MPI while a significant negative correlation between IACT and PEFR.

Conclusions: Asthmatic children were associated with higher RA dimensions, impaired RV function, higher IRCT and IACT. There was a positive correlation between IRCT and PWD, PEFR and MPI.

Keywords: Atrial Electromechanical Delay; Tissue Doppler Echocardiography; Children. Asthma.

Introduction

Bronchial asthma is a prevalent chronic illness in children. Worldwide, the prevalence of childhood asthma has been rising. In a similar vein, persons with asthma now experience an increasing prevalence of atrial fibrillation (AF) ^[1].

Corticosteroids and β 2-adrenergic receptor agonists are the two main medications used for asthma sufferers. Research indicates that individuals with asthma who receive treatment with β 2-adrenergic receptor agonists had an increased frequency of arrhythmias ^[2]. Agonistic β 2-adrenergic receptors, such as inhaled salbutamol, can modify the conduction of cardiac electrophysiology ^[3].

Salbutamol produces favorable chronotropic effects in addition to improving atrioventricular nodal conduction and lowering ventricular, atrial, and nodal refractoriness ^[4]. These changes may have a role in the development of arrhythmias that occur. However, other etiologies may also contribute to cardiac arrhythmia. The atrial electrical properties that are continuous and inhomogeneous may be affected by atrial stretching and expansion. Right ventricle (RV) hypertrophy and dilatation can result from pulmonary arterial hypertension, which can be brought on by chronic bronchial asthma. Right ventricular hypertrophy was associated with both diastolic and systolic dysfunction ^[5].

The degree of right ventricular hypertrophy and total pulmonary resistance determines the degree of right ventricular diastolic dysfunction. These pathological states may interfere with the right atrium's electrical functions ^[6]. The atrium's electrical anomalies may make

atrial fibrillation more likely ^[1]. P-wave dispersion (PWD) and atrial electromechanical delay (AED) are elevated in bronchial asthma due to these anomalies.

A measure of the inhomogeneous propagation between the left and right atrial tissues is called PWD. A higher risk of AF is associated with increased AED and PWD ^[7, 8]. For evaluating ventricular diastolic dysfunction, the most effective non-invasive techniques are tissue doppler imaging (TDI) and pulse doppler wave (PWD) ^[9, 10].

Two helpful methods that offer a numerical assessment of regional cardiac function are PWD and TDI. Even in cases where routine echocardiogram measurements are normal, PWD and TDI data can identify subclinical right ventricular dysfunction in the early stages of the disease ^[7].

Asthma is a chronic inflammatory disease of the airways. It may cause pulmonary arterial hypertension, which causes RV hypertrophy and dilatation, RV systolic and diastolic dysfunction. The level of right ventricular dysfunction depends on the degree of right ventricular hypertrophy and total pulmonary resistance ^[11].

The aim of this work was to assess AED using tissue doppler echocardiography in children with asthma.

Patients and Methods

This case-control study was carried out at the Pediatric Department of Benha University Hospital from 1st April 2022 to 1st March 2024. The study involved 40 children, aged 8 to 16 years, of both genders, diagnosed with asthma. Diagnosis was made depending on recurring episodes of cough, wheezing,

breathlessness, and chest tightness, which were responsive to β_2 agonists. Furthermore, all the participants demonstrated reversible airflow limitation, defined as a minimum of 12% improvement in forced expiratory volume in the 1st second (FEV1) after the use of a short-acting β_2 -agonist [12]. The control group comprised 40 healthy children, matched by age and sex. The study was approved by the Ethical Committee of Benha University Hospitals {M.S.11.1.2022}, Egypt, and informed written consent was obtained from the parents or guardians of the participants.

Exclusion criteria include other chronic lung disease, cardiac disease as congenital heart disease, rheumatic heart disease and cardiomyopathy, taking anti arrhythmic drugs and age ≤ 8 years.

Patients were divided into two equal groups: Patients group: children complaining of bronchial asthma and control group: healthy children.

All the patients were subjected to complete history taking, physical examination and spirometry testing.

Spirometry Testing

A comprehensive physical examination and spirometry were performed according to the consensus standards set by the European Respiratory Society (2). The pulmonary function testing was administered to all the subjects using spirometry (peak expiratory flow rate (PEFR) forced expiratory volume 1 (FEV1), forced vital capacity (FVC), and the ratio of FEV1 to FVC.

Echocardiographic and Tissue Doppler Echocardiographic Measurements

In the apical four-chamber view, the pulse wave doppler parameters were applied to mitral and tricuspid valves; peak early diastolic (E) flow, peak late diastolic (A) flow, E/A ratio, and E-DT were measured. All indices were average for three consecutive beats. The sampling volume was placed parallel to the myocardial flow as closely as possible. In the apical four-chamber view, TDI was performed from free wall RV. The TDI parameters were measured from the lateral tricuspid annulus. The peak early velocities (E'), late diastolic velocities (A'), E'/A' ratio, isovolumetric relaxation time (IVRT), S'-wave velocities, and myocardial performance index (MPI) was recorded. All indices were average for three consecutive beats.

Atrial Electromechanical Delay Measurements:

The time intervals from the onset of the P wave on ECG to the beginning of the A'-wave (PA) representing atrial electromechanical delay (AED), were obtained from the lateral mitral annulus, septal mitral annulus, and RV tricuspid annulus. These time intervals were termed the lateral PA, septal PA, and RV PA, respectively. The intra-right atrial conduction time (IRCTecho) was measured as the difference between septal PA and RV PA (septal PA–RV PA). The intra-left atrial conduction time (ILCT-echo) was also measured as the difference between lateral PA and septal PA (lateral PA–septal PA). The interatrial conduction time (IACT-echo) was estimated as the difference between lateral PA and RV PA (lateral PA–RV PA [13].

P-Wave Dispersion Measurement:

The maximum and minimum P-wave durations were measured from the 12-lead surface electrocardiogram. PWD was calculated as the difference between the maximum and minimum P-wave durations [14]. An acceptable electrocardiogram was determined by its ability to measure the P-wave duration in at least 8 of the 12 electrocardiographic leads recorded simultaneously.

Statistical analysis

Statistical analysis was done by SPSS v26 (IBM Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD) and were compared between the two groups utilizing unpaired Student's t-test. Qualitative variables were presented as frequency and percentage (%) and analyzed using the Chi-square or Fisher's exact test when appropriate. Correlations between various variables were done using Pearson moment correlation equation. A two-tailed P value < 0.05 was considered statistically significant.

Results:

Demographic data, SBP and DBP of the patients were insignificantly different from those of the controls. On the other hand, pulse rate and respiratory rate were significantly higher in the asthma group compared to the control (P<0.05). FVC, FEV1, FEV1/FVC ratio and PEFr were significantly lower in the asthmatic

patients as compared to the controls (p< 0.001). **Table 1**

The median duration of illness was 4 years with a range between 1 and 10 years. All the patients received SABA while 31 patients (77.5%) received ICS, and 4 patients (10%) were treated with LTRA. Regarding the severity of asthma, intermittent asthma was reported in 15 patients (37.5%), mild asthma in 11 patients (27.5%), moderate degree in 7 patients (17.5%) and severe degree in 7 patients (17.5%). **Table 2**

RVE, RV E\A ratio, RV DT, FS, tricuspid S, tricuspid E and tricuspid A were insignificantly different between the patients and the control groups. The dimension of RA (either major or minor), ICT, IRT, ET and MPI were significantly higher in the asthmatic group (p<0.05). The RV TAPSE and ICT were significantly lower in the asthmatic group (P<0.05). Left side measurements showed no significant difference. **Table 3**

PWD was significantly higher in the asthmatic group (p= 0.003). Septal PA, lateral PA and ILCT were insignificantly different between the patients and the control groups. The RV PA, IRCT and IACT were significantly higher in the asthmatic group (p<0.05). **Table 3**

There was a significant positive correlation between IRCT and age, severity of asthma, duration of illness, ICT and IRT while there was a significant negative correlation between IRCT with PEFr. **Table 4**

Table 1: Demographic data, vital signs and respiratory functions of the studied groups

Variables	Patients group (n=40)	Control group (n=40)	Test of significance	P value	
Age (years)	9.60 ± 3.26	10.15 ± 2.33	- 0.869	0.387	
Sex	Male	20 (50%)	r = 0.151	0.823	
	Female	20 (50%)			19 (47.5%)
Height (cm)	135.43±18.81	139.03±11.05	-1.044	0.300	
Weight (kg)	37.88±16.30	39±15.01	- 1.162	0.240	
BSA (m2)	1.18±0.33	1.21±0.25	- 0.769	0.410	
SBP (mmHg)	94.75±7.32	93.74 ± 6.30	0.714	0.432	
DBP (mmHg)	64.70±6.22	63.75±6.30	0.679	0.499	
Pulse rate (breaths/min)	98.65±7.20	94.83±6.08	2.567	0.012*	
Respiratory rate (cycles/min.)	21.95±2.18	17.83±1.91	6.094	0.001*	
Respiratory functions	FVC (liters)	43.80 ± 4.58	58 ± 5.61	- 12.410	< 0.001*
	FEV1 (liters)	53.45 ± 7.32	89.08 ± 3.36	- 27.981	< 0.001*
	FEV1/FVC (%)	72 ± 6.67	92.18 ± 3.37	- 17.068	< 0.001*
	PEFR (L/min)	33.90 ± 6.94	59.58 ± 2.69	- 21.813	< 0.001*

BSA: Body surface area, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, FVC: Forced vital capacity, FEV1: Forced expiratory volume 1, PEFR: Peak expiratory flow rate.

Table 2: Characteristics of asthmatic patients

Characteristics	Patients (n=40)	
Duration of illness (years) (median (IQR))	4 (1-10)	
Asthma treatment	SABA	40 (100%)
	ICS	31 (77.5%)
	LABA	0 (0%)
	LTRA	4 (10%)
Degree of asthma severity	Intermittent	15 (37.5 %)
	Mild	11 (27.5%)
	Moderate	7 (17.5%)
	Severe	7 (17.5%)

IQR: Inter quartile range, SABA: Short-acting beta-agonists, ICS: Inhaled corticosteroids, LABA: Long-acting beta agonists, LTRA: Leukotriene receptor antagonists.

Table 3: Conventional ECHO and Tissue Doppler Findings in the Studied Groups, and Comparison of P-wave Parameters and Atrial Electromechanical Delay

Variables	Patients group (n=40)	Control group (n=40)	Test of significance	P
Conventional Echo				
RA Major (cm)	3.34±0.41	3.07±0.43	2.847	0.006*
RA Minor (cm)	3.26±0.38	3.04 ± 0.51	2.121	0.037*
RV TAPSE	1.80±0.12	1.89±0.17	-2.885	0.012*
RV E	64.71±14.31	64.46±15.07	0.076	0.940
RV A	53.02 ± 12.14	54.33±11.99	0.485	0.629
RV E\A ratio	1.29 ± 0.36	1.26±0.38	0.393	0.696
RV DT	135.58±30.48	142.50±33.39	0.969	0.336
FS	40.74 ± 6.41	42.10 ± 7.72	-0.857	0.394
Tissue doppler findings				
Tricuspid S	12.68 ± 2.10	12.10±0.80	1.629	0.107
Tricuspid E	14.73 ± 3.29	14.19±1.19	0.986	0.327
Tricuspid A	8.60 ± 2.39	9.21±1.06	-1.493	0.140
ICT	48.45±5.49	42.38±7.17	2.854	0.006*
IRT	44.28±7.18	41.33±5.06	2.214	0.037*
ET	297.23±34.44	281.9 ±16.87	2.527	0.014*
MPI	0.32±0.05	0.30±0.03	2.159	<0.001*
Comparison of P-wave parameters and atrial electromechanical delay				
P-min (ms)	44.78±4.92	42.43±4.60	1.269	0.208
P-max (ms)	87.53±8.01	85.60±7.35	1.119	0.266
PWD (ms)	48.33±5.19	43.48±4.87	3.015	0.003*
Septal PA (ms)	38.30±7.26	38.75±4.70	t =- 0.329	0.743
RV PA (ms)	28.55±6.86	23.18±4.56	t =4.129	< 0.001*
Lateral PA (ms)	42.68±4.73	41.65±7.78	t =0.712	0.479
IRCT (Septal-RV)	14.75±3.87	9.65±2.43	t =7.049	< 0.001*
ILCT (Lateral-Septal)	17.20±2	16.80±2.09	Z= 0.874	0.385
IACT (Lateral-RV)	27.63±9.28	22.03±6.54	Z= 3.121	0.003*

Data are presented as mean ± SD. * Significant p value <0.05, t: Independent samples t-test, z: Mann-Whitney u-test, RA: right atrium, RA: Right atrium, E\A: ratio of peak velocity blood flow from Right ventricular relaxation in the early diastole (E wave) to peak velocity flow in late diastole caused by atrial contraction (A wave), TAPSE: Tricuspid Annular Plane Systolic Excursion, RV: right ventricular, DT (deceleration time), FS: Fractional shortening, Tricuspid E(Annular peak velocity during early diastole); Tricuspid A (Annular peak velocity during late diastole); Tricuspid S(Annular peak velocity during systole); ICT: isovolumic contraction time, IRT: isovolumic relaxation time, ET(ejection time), MPI(myocardial performance index), P-min: Minimum P-wave duration, P-max: Maximum P-wave duration, P-WD: P- wave dispersion. Septal PA: Electromechanical delay between P wave in ECG and A wave in tissue Doppler in echocardiography at septum, RV PA: Electromechanical delay between P wave in ECG and A wave in tissue Doppler in echocardiography at RV wall, Lateral PA: Electromechanical delay between P wave in ECG and A wave in tissue Doppler in echocardiography at lateral Left ventricular wall, IRCT: Intra-right atrial conduction time, ILCT: Intra-left atrial conduction time, IACT: Inter atrial conduction time.

Table (4): Correlation between IRCT with other variables

Variables	Sperman's correlation coefficient	P value
Age (years)	0.362	0.015*
Severity of asthma	0.433	0.004*
Duration of illness	0.638	< 0.001*
PEFR	-0.395	0.010*
P wave dispersion	0.108	0.34
TAPSE	-0.155	0.169
Tricuspid S	-0.001	0.992
Tricuspid E	-0.040	0.723
Tricuspid A	0.112	0.321
ICT (ms)	0.225	0.044*
IRT (ms)	0.30	0.006*
ET	0.163	0.147
MPI	0.176	0.117

*: Statistically significant ($p < 0.05$), , PEFR: Peak expiratory flow rate. TAPSE: Tricuspid annular plane systolic excursion, Tricuspid A (Annular peak velocity during late diastole); Tricuspid S(Annular peak velocity during systole); ICT: isovolumic contraction time, IRT: isovolumic relaxation time, MPI(myocardial performance index) ET(ejection time).

Discussion

Asthma is a chronic inflammatory disorder of the airways characterized by airflow limitation. This limitation may be completely or partially reversed with or without specific therapy. The prevalence of asthma has been increasing among children^[15].

In the current study, the pulse rate and respiratory rate were significantly higher in the asthma group as compared to the controls. Supporting our results, researchers^[16] showed that asthma control, assessed by asthma control test, influenced the heart rate. The control group showed better heart rate recovery when compared with the controlled asthma group and with the partial or uncontrolled asthma group. In disagreement with our result, Baysal and Has^[17] found that the heart rate was insignificantly different between both groups. Including adult individuals in their study may explain the difference from our results. Also, Zeybek and colleagues^[18] found that heart rate was insignificantly

different between both groups. The lower weight in their patients may explain this difference.

In the present study, the median duration of illness was 4 years with a range between 1 and 10 years. All the patients received treatment with SABA while 31 patients (77.5%) received ICS, and 4 patients (10%) were treated with LTRA. Regarding the degree of severity of asthma, intermittent asthma was reported in 15 patients (37.5%), mild asthma in 11 patients (27.5%), moderate degree in 7 patients (17.5%) and severe degree in 17 patients (17.5%). Supporting our results, Wagdy and co-workers^[19] showed that 28.3% of patients presented with mild asthma, 45.71% moderate asthma, and 25.7% suffered from very severe bronchial asthma. Also, Zeybek and colleagues^[18] found that out of 51 patients, 33 (64.7%) had mild asthma and 18 (35.3%) had moderate and severe asthma. In addition, Zeigerand colleagues^[20] found that the

median duration of asthma was 4.8 years with a range between 0.3 and 12.1 years.

In our study, the FVC, FEV1, FEV1/FVC ratio and PEFR were significantly lower in the asthmatic patients as compared to the control group. Supporting our result, Wagdy and co-workers^[19] showed that FEV1 was significantly lower in the asthmatic patients as compared to the control group. In the same line,^[17] found that FVC and FEV1 were significantly lower in the asthmatic patients than in the control group. But in contrast, they found that FEV1/FVC ratio and PEFR were insignificantly different in both groups. Also,^[21] showed that FVC, FEV1, FEV1/FVC ratio and PEFR were significantly lower in the asthmatic patients than in the control group.

In the present study, the dimensions of the RA (either major or minor) were significantly higher in the asthmatic group. Also, P-wave dispersion was significantly higher in the asthmatic group. The RVE TAPSE was significantly lower in the asthmatic group than in the control group. On the other hand, there was no statistically significant difference between the patients and the control groups regarding RVE, RV E/A ratio and RV DT. Supporting our result, Karasu and Aydıncak^[22] found that most of conventional echocardiographic parameters measuring RV function were impaired in patients with asthma compared to control subjects.

In the present study, there was no statistically significant difference between the patients and the control groups regarding LA major axis, mitral E, mitral A, mitral E/A ratio, mitral E-DT, LVEF and FS. Also, Wagdy and co-workers^[19] found that there was no statistically significant difference between the patients

and the control groups regarding the LVEF and FS. Supporting our result,^[17] showed that there was no statistically significant difference between the patients and the control groups regarding mitral E, mitral A, mitral E/A ratio, mitral EDT and LVEF. Also, Ghandi and colleagues^[21] found that the dimensions of RA (either major or minor) were insignificantly different when comparing the two groups.

In the present study, tissue doppler imaging shows that ICT, IRT, ET and MPI were significantly higher in the asthmatic group than in the control group. On the other hand, there was no significant difference between the patients and the control groups regarding the tricuspid S, tricuspid E, and tricuspid A. Supporting our result^[17] found that there was no significant difference between the patients and the control groups regarding the tricuspid S, tricuspid E, and tricuspid A. Also, Ciftel and colleagues^[23] showed that there was no significant difference between the patients and the control groups regarding the tricuspid S, tricuspid E, and tricuspid A. In contrast, Ghandi and colleagues^[21] showed that the tricuspid S and tricuspid E were significantly higher in control group than in the asthmatic group, and tricuspid A was significantly higher in asthmatic group than in the control group.

In the current study, there was no significant difference between the patients and the control groups regarding septal PA, lateral PA and ILCT. On the other hand, the RV PA, IRCT and IACT were significantly higher in the asthmatic group. Supporting our study, Baysal and Has^[17] found that septal PA and lateral PA were significantly higher in the asthmatic group than in the control group. On the same line, Ghandi and colleagues^[21] found that

there was no significant difference between the patients and the control groups regarding septal PA, lateral PA and ILCT. Also, the RV PA, IRCT and IACT were significantly higher in the asthmatic group than in the control group. Also, Ciftel and colleagues ^[23] found that septal PA and lateral PA were significantly higher in the asthmatic group.

In the present study, there was a significant positive correlation between IRCT and age, severity of asthma, duration of illness, ICT and IRT while there was a significant negative correlation between IRCT and PEFR. There was a significant positive correlation between IACT with Tricuspid S and MPI while there was a significant negative correlation between IACT with PEFR. In the same line, Ciftel and colleagues ^[23] found that the IRCT increased in patients with asthma and there was a correlation between the increase in the intra-right atrial conduction time and Right ventricular dysfunction.

Limitations

limitations included single center study may result in different findings than elsewhere, small sample size that may produce insignificant results and we are not able to follow up for a long period of time to correlate effective parameters of atrial electromechanical delay with the development of arrhythmia. So, we recommend studies on larger numbers of patients to divide the patients into subgroups with different medications to assess the effect on the cardiovascular function and to correlate the results of atrial electromechanical with the medications.

Conclusions

Asthmatic children had RV function impaired (systolic and diastolic) detected by MPI. Also, there was atrial electromechanical delay detected by higher IRCT, ICT and P wave dispersion. There were positive correlations between IRCT and age, severity of asthma, duration of illness, ICT and IRT while there was a negative correlation between IRCT and PEFR. Also, there was positive correlations between IACT and Tricuspid S and MPI while there was a negative correlation between IACT with PEFR. Also, there were positive correlations between IACT and Tricuspid S and MPI while there was a negative correlation between IACT with PEFR.

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