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Evaluation of the Ventricular Function Based on Echocardiographic Findings in Asthmatic Children

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Abstract

Background: Objective: Asthma is a chronic inflammatory disease leading to hypertrophy and dilatation of the right ventricle. This study aims to evaluate and compare left and right ventricular systolic and diastolic functions of the heart based on echocardiographic criteria in children with moderate to severe asthma and non-asthmatic children referred to Hazrat Rasouland Firoozabadi Hospitals of Tehran in 2019.

Methods: In this case-control study, 50 patients with a definite diagnosis of moderate to severe asthma (case group) and 50 healthy individuals (control group) were studied and compared in terms of clinical and echocardiographic measures. Blood pressure, heart rate, body height and weight of all children were recorded. The patients who were >6 years underwent pulmonary function tests using spirometry. Conventional and TDI echocardiography was performed by a single experienced pediatric cardiologist on the two groups blindly and echocardiographic data was collected.

Results: The results showed that the left ventricular stroke volume was significantly lower in patients with asthma. Also, in the right ventricular SV, significantly lower values were found in the group of patients under study than healthy individuals (P=0.01). The E/A ratio in both groups was higher than one; the mean and standard deviations were not significantly different between the case (1.72±0.26) and the control group (1.92±0.32).

Conclusion: The results of this study showed that asthma can affect ventricular contraction in children. Contrary to the previous studies and despite the observation of cardiac systolic dysfunction in patients with asthma, diastolic dysfunction in these patients was not observed even by Tissue Doppler echocardiography.

Key Words: Asthma, Cardiac function, Echocardiography.

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1- INTRODUCTION

Asthma is a chronic inflammatory disease of the airways which is related to hyper responsiveness, and is characterized with recurrent wheezing, coughing and breathlessness characterized by an obstruction of airflow, which may be completely or partially reversed with or without specific therapy (1). Bronchial asthma affects many organs including the heart. There are many explanations for the occurrence of cardiac dysfunction in asthmatic children (2-4).

Echocardiography has detected RV systolic and diastolic dysfunctions in a considerable number of asthmatic children -even in mild cases; and Left ventricular dysfunction is usually detected in severe asthmatic cases. However, these cardiac dysfunctions may be reversible especially in acute cases (5, 6). Many suggested that chronic hypoxia may cause pulmonary arterial hypertension, which causes RV hypertrophy and/or dilatation (2). Some studies have proposed that recurrent hypoxemia and the release of various mediators and cytokines in patients may cause chronic inflammation, which could induce pulmonary vasoconstriction (3, 4).

It is hypothesized that the exaggerated respiratory efforts may raise intrathoracic pressure that increases RV afterload and pulmonary hypertension with RV hypertrophy and/or dilatation. As a result, pulmonary hypertension occurs leading to RV hypertrophy and/ or dilatation (3, 4, and 7). Consequently, the RV hypertrophies and dilates due to chronic pressure overload lead to both systolic and diastolic dysfunction (7). Increased LV afterload and decreased LV preload and thus LV dysfunction occur due to Interactions between the RV and LV (8).

There are important limitations to determining RV function by conventional echocardiography (9). The position of the RV at the back of the sternum causes poor image quality. Also, locating the endocardial boundary of the anterior wall is a problem, because of the thicker trabeculations as compared with the LV. Furthermore, the RV cavity has a more complex geometry than the LV, and RV performance depends on extrinsic conditions, such as afterload, preload, and LV performance (10). Although there are many noninvasive diagnostic modalities of ventricular function, right ventricular function remains difficult and challenging to quantify. Conventional imaging techniques such as radionuclide ventriculography and standard echocardiography have limitations when applied to the right ventricle. Radionuclide ventriculography involves exposure to radiation, is relatively expensive, has restricted availability, and is not easily repeatable (11).

Thus, this study aims to investigate ventricular diastolic and systolic functions, by using Tissue Doppler Imaging (TDI) and conventional echocardiography in asthmatic children, using regular inhaled corticosteroid, without any cardiovascular symptoms.

2- MATERIALS AND METHODS

2-1. Population and Procedures

We studied 50 pediatric patients (28 males and 22 females), selected randomly from those with bronchial asthma referring to our hospital for routine checkup, and 50 healthy subjects were selected randomly from their families. Inclusion criteria included all patients meeting the criteria for bronchial asthma. Exclusion criteria encompassed patients with comorbid diseases, such as upper or lower respiratory infection, allergic rhinitis, gastroesophageal reflux, obesity, chronic cardiovascular or pulmonary diseases and acute asthma attack during the last 4 weeks.

All the children in the study were subjected to full history taking. Complete physical examinations were performed by the same physician. Blood pressure (BP), heart rate (HR), Body height and weight of all children were recorded. The patients who were >6 years underwent pulmonary function tests using spirometry forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and the ratio of FEV1 to FVC, which were all documented. The ethics committee of the university approved the study and informed consent forms signed by the parents were obtained.

All asthmatic patients involved in this study were suffering from moderate to severe stable asthma and had received inhaled corticosteroid treatment for different periods of time and doses. Transthoracic echocardiography was done using TDI and the conventional method by a single experienced pediatric cardiologist for all the included patients and healthy group. and the following parameters were obtained and estimated: LV mass (LVM, g) according to the formula of Devereux (12), stroke volume (SV), ejection fraction (EF, %), fractional shortening (FS, %), ratio between heights of early and late diastolic flow velocity peaks (E/A ratio) for both mitral and tricuspid valves, deceleration time (DT, ms), LV and RV relative wall thickness (LVRWT, RVRWT, mm),as well as tricuspid annular plane systolic excursion (TAPSE).

LV fractional shortening (FS) was calculated as LVVDLVDS/ LVDD (13). For ventricular diastolic function evaluation, DT and E/A were used. The ratios of E to A were estimated for mitral and tricuspid valves (14).

2-2. Statistical Analysis

The data were analyzed using SPSS software (version 22.0). Kolmogorov–Smirnov and Shapiro Wilk tests were used to assess normality of the distribution. Parametric variables were compared using the Student's t-test for normally distributed data and the Mann Whitney U test for not normally distributed data. Bivariate associations of the variables were assessed using Pearson's correlation coefficients. Variables were expressed as mean ±SD and p-value<0.05 was considered to indicate statistical significance.

2-3. Ethical Considerations

Before the intervention, the goals of the study were fully explained to the patient's parents, then, if agreed, informed consent was obtained from them. In this study, all researchers were committed to the Helsinki Statement. This clinical trial study was approved by the Ethics Committee of Iran University of Medical Sciences (ID-number: IR.IUMS.REC.1400.098).

3- RESULTS

We studied 50 patients (28 boys and 22 girls) with a mean age of 10.55±3.02 years who were previously diagnosed with bronchial asthma. The characteristics of the children and healthy subjects are shown in **Table 1**.

Table-1: Comparison (mean ± SD) of clinical characteristics

Variable	asthmatic children (n=50)	Healthy control (n=50)	P value
Age (years	10.55± 3.02	11.09 ± 3.21	0.260
Body height (cm)	142.8 ± 12.2	142.5 ± 12.4	0.110
Body weight (kg)	27.6 ± 12.5	28.6 ± 12.5	0.479
Systolic BP (mmHg)	104.80 ± 8.94	103.78 ± 9.47	0.350
Diastolic BP (mmHg)	64.06 ± 5.88	62.38 ± 9.63	0.167
Heart rate (bpm)	84.55 ± 14.93	87.42 ± 10.87	0.457

- Analyzed with Student's t test, Man-Whitney u test, Chi-square test

The spirometry findings are summarized in **Table 2**. There were no statistically significant differences in age, weight, heart rate, systolic and diastolic blood pressures between bronchial asthma patients and the controls.

Table-2: Spirometry findings of asthmatic patients

variable	max	min	mean ± SD
FEV1	94.9	70.6	82.7 ± 12.1
FVC	100.6	83.8	92.2 ± 8.4
FEVI/VC	99.3	80.1	89.7 ± 9.6

Left and right chambers echocardiographic findings are listed in **Table 3**. **Table3** shows that there were no statistically significant difference in the echocardiographic indices of RV and LV dimensions between the two groups. Left ventricle fractional shortening (LVFS) and Light ventricle ejection fraction (LVEF) didn't also differ, significantly, between the two groups (p=0.165 and p=0.162). Left ventricle stroke volume (LSV) and Right ventricle stroke volume (RSV) were significantly lower in the asthmatic group (p=0.02 and p=0.01)

In the analysis 4(8%) of the asthmatic group were diagnosed with mild pulmonary arterial hypertension and one (2%) with moderate PAH, while in the meta analyses we didn't find any significant differences between the two groups of our study.

4- DISCUSSION

Asthma is the most common cause of respiratory disability in children. [3]Bronchial asthma not only affects the lung but also affects other organs including the heart. Even with mild cases, subclinical cardiac dysfunction can be documented and the severity of cardiac affection is parallel to the severity of the disease. LV diastolic dysfunction was observed in severe BA. The occurrence of supraventricular tachycardia in BA is related to the presence of interventricular septal hypertrophy, LV dysfunction, and increased PAP (15).

According to other studies, even in mild cases, right ventricular (RV) systolic and diastolic dysfunction were diagnosed by echocardiography, while left ventricular (LV) dysfunction usually presents itself in severe asthmatic cases which may be reversible in acute conditions (5, 6). Thus, the present study aimed at evaluating and comparing left and right ventricular systolic and diastolic function of the heart based on echocardiographic criteria in children with moderate to severe asthma and non-asthmatic children referred to Hazrat Rasoul and Firoozabadi Hospitals of Tehran in 2019.

Previous studies have found no statistically significant difference between children with asthma and the control individuals in terms of heart rate and systolic and diastolic blood pressure. The results of our study are consistent with the results of these studies (10, 16, 17). Reported by some echocardiographic studies, even in mild cases, right ventricular (RV) systolic and diastolic dysfunctions were present. On the other hand, left ventricular (LV) dysfunction usually presents itself in severe asthmatic cases which may be reversible in acute conditions (5, 6).

In the present study, there were no significant differences in the echocardiographic indices of RV dimensions and functions between the two groups (RV wall thickness, RV diameter, Evelocity, A velocity, E/A velocity ratio) that was comparable to the previously published normal values (18,19). These findings are corresponding to the study done by Mahmoud et al. (17) who evaluated ventricular function based on myocardial performance index (MPI).

Table-3: Echocardiographic data comparison (mean ± SD)

Variable		Asthmatic children	Healthy controls	P value
LA/AO		0.91±0.19	0.91±0.19	0.23
SEPTAL(E)		15.1±2.4	14.8±2.6	0.12
SEPTAL(A)		5.7±1.8	5.92±2.05	0.133
SEPTAL(S)		8.4±1	8.6±1.4	0.165
Lateral(E)		19.6±3.2	19.2±3.8	0.264
Lateral(A)		6.75±1.35	6.6±1.1	0.177
Lateral(S)		11.3±2.2	11.25±1.05	0.225
E		181±29	185±24	0.112
A		71±10	72±15	0.123
E/A		1.72±0.26	1.92 ± 0.32	0.17
DT		197.95±67.95	191.50 ± 45.50	0.450
Lad max		25.5±4.8	25.7±4.7	0.055
LA area1		11.55±2.65	10.45±2.05	0.221
LA area2		14.0±3.3	16.75±5.25	0.343
TRPG		31±7	31.7±7.7	0.087
RVIDd		14.2±2.8	13.2±2.9	0.122
IVSd		5.2±0.8	5.3±0.9	0.077
LVIDd		34.8±4.5	34.9±3.5	0.087
LVPWd		5.2±0.9	5.3±0.9	0.091
LVIDs		20.9±5.2	20.8±4.2	0.122
LVmass		55.7±11.3	69 ± 18.26	0.223
RV1		33±7	33.5±5.5	0.066
RV2		25.3±5.2	28±7	0.443
RV3		74±7	72.5±7.7	0.349
TAPSE		2.11±0.11	2.15 ± 0.32	0.35
RVWT		0.47 ± 0.12	0.47 ± 0.15	0.066
RSV		50.01 ± 19.25	64.71 ± 23.66	0.01
LVWT		0.40 ± 0.077	0.34 ± 0.055	0.071
LV FS		0.36±0.8	0.34 ± 0.05	0.165
LV EF		0.66 ± 0.11	0.63 ± 0.08	0.162
LSV		40.74 ± 15.27	50.98 ± 13.08	0.02
DD	Normal	47 (94%)	49 (98%)	0.451
	Mild	3(6%)	1(2%)	0.43
	Moderate	0	0	
	Severe	0	0	
PAH	No	45(90%)	49(98%)	0.341
	Mild	4(8%)	1(2%)	0.44
	Moderate	1(2%)	0	
	Severe	0	0	

LA/AO, Left atrium to aortic root diameter ratio; LAE, left atrium enlargement; E/A, E wave to A wave ratio, TRPG, Tricuspid regurgitation peak gradient; RVIDd, Right ventricular internal dimension diastolic; IVSd, Interventricular septal end diastole; LVIDd, Left ventricular internal diameter end diastole; LVPWd, Left ventricular posterior wall end diastole; LVIDs, Left ventricular internal diameter end systole; LV-FS, Right ventricle fractional shortening; LV-EF, Left ventricle ejection fraction; TAPSE, Tricuspid annular plane systolic excursion; RSV, Right ventricle stroke volume; LSV, Left ventricle stroke volume; RVWT, Right ventricular wall thickness; LVWT, Left ventricular wall thickness; RV-EF, Right ventricle ejection fraction; RV-FS, Right ventricle fractional shortening; PAH, Pulmonary arterial hypertension. Analyzed with Student's t test, Man-Whitney u test, Chi-square test

The results of the study by Elmasry et al. (20) showed that the dimensions of right ventricular echocardiography did not differ significantly between patients with asthma as compared to controls, which is consistent with those of the present study. But Alpaslan et al. (21) as well as Chicherina et al. (15) stated that right ventricular diastolic dysfunction is the first hemodynamic change in bronchial asthma that contradicts the results of our study. Also Eniseeva et al. (22) reported that in patients with bronchial asthma, the extent of right ventricular dysfunction depends on right ventricular hypertrophy and overall lung resistance.

This could be explained by the younger age of our study group and the well-controlled asthma in our patients, which might have affected the clinical and echocardiographic results in regard to chronic lung diseases. Some studies reported that there were no differences in echocardiographic findings regarding the ventricular function with the exception of RV wall thickness (16, 23) and some even reported no difference between the two groups regarding RVWT and LVWT (10). In our study, we didn't find any difference between the two groups in RVWT and LVWT parameters.

EF, FS, TAPSE, and SV values of both ventricles were evaluated to assess ventricular systolic function. EF and FS were similar in both groups with no significant differences. TAPSE also didn't show any significant differences in asthmatic patients, in contrast to the study done by Özkan (10) who reported lower TAPSE in asthmatic patients.

Hedlin et al. (24) reported that SV decreased in asthmatic patients whose asthma was provoked by exercise and increased with inhale salbutamol. Present study showed that the SV of both the LV and RV were lower in asthmatic children than in the controls, while our study didn't include exercise and challenge tests.

To assess LV contractility, studies analyzed changes in LV VCFc and afterload (ESWSm) (25). The ventricular contractility and myocardial performance may be affected by chamber geometry, which need to be identified by measuring ESWSm, VCFc-midwall and MFS. ESWSm which is accepted as afterload, is dependent on both chamber shape and mass/volume ratio, presents the forces opposing predominantly meridional and circumferential planes. This is an index of total forces per unit of myocardium; and, therefore, may cause an underestimation in true afterload [18]. MFS, as representative of fiber afterload, seems to be a more accurate index of afterload in hypertrophied or dilated LV (26).

We used tricuspid E/A, E, A, DT, by using conventional echocardiography and TDI to evaluate ventricular diastolic function. There are some studies which reported RV and LV diastolic dysfunction in patients with moderate to severe asthma (2, 15, and 27). In contrast to these studies, we didn't diagnose any significant diastolic dysfunction in asthmatic patients, because tricuspid E/A values were >1 without any sign of pseudo-normal E/A values.

In evaluation of LAE also no significant differences between the two groups were found and our findings showed that there was no diastolic dysfunction among our asthmatic children. This result may due to use of inhaled corticosteroids.

Zeybek et al. (6) showed that lateral annular velocities of tricuspid and IVRT were different between asthmatic children and controls. Shedeed (16) reported that IVRT and IVCT were significantly greater in asthmatic children as detected by TDI.

Some studies suggested that LV diastolic function is impaired in patients with bronchial asthma despite it had no effect on RV diastolic function (28).

Making the diagnosis of PAH in children poses several challenges. Due to the low prevalence of PAH, general pediatricians have limited experience of/exposure to the subtle symptoms which often mimic other more common cardio-respiratory conditions such as asthma (26).

In patients with bronchial asthma, when blood pressure in the pulmonary artery is measured, very often hypertension is registered. Since patients with bronchial asthma are hyperventilating, this pulmonary hypertension is not secondary to hypoventilation, as in patients with chronic bronchitis or pulmonary emphysema. The pulmonary hypertension in them must be therefore classified as primary. It is probable that its origin is in an allergic vasoconstriction of the pulmonary artery, occurring simultaneously with the well-known bronchoconstriction. In our study, there were no significant differences in the two groups regarding the measurement of pulmonary arterial pressure while the findings of some other studies are incongruent with this result (29).

In the present study, due to restrictions, respiratory tests were only conducted on the patient group, but in some other studies in which both groups were tested, FEV1 was positively correlated with IVRT and ET-MV; and PEF was negatively correlated with RVWI and LVWI. Ozdemir et al. (23) reported that PEF was negatively correlated with tricuspid E'/A', while Sheeded et al. (16) demonstrated a negative correlation between PEF and IVRT. Inhaled corticosteroids exert a strong anti-inflammatory effect on airways; they represent the most effective agents for long-term asthma control (30).

Some studies have revealed that inhaled corticosteroids have protective effects on cardiac function in asthmatic patients (31). A previous study showed that the asthmatic children who used inhaled corticosteroid underwent a decrease in arterial stiffness, and an increase in dispensability and strain (18).It is suggested that inhaled corticosteroids could have certain protective effects in asthmatic children. The mechanism possibly is that the decrease in arterial stiffness involves nitric oxide synthesis and vasodilatation (32).

In the study that evaluated right ventricular dysfunction in intermittent and persistent mildly asthmatic children and serum NT-proBNP, increased serum NT-proBNP was associated with subclinical RV dysfunction and RV function was significantly affected in children with bronchial asthma (33).

In another study comparing heart function, baseline physical activity level, and functional exercise capacity in young patients with mild-to-moderate asthma and healthy controls, Changes in echocardiographic were observed in mild-to-moderate asthma patients even with a normal functional exercise capacity and baseline physical activity level (34).

In a different study, cardiac function was evaluated after 4-6 weeks of treatment with inhaled steroid and beta-2 agonist; they found significant improvement of right ventricular diastolic filling parameters by Doppler echocardiography after the treatment in children with asthma (27).

Aoki et al. evaluated the chronic effects of theophylline on cardiac function concluding that theophylline appears to have a minimal effect on resting cardiac function, but a possibly deleterious effect on the cardiac response to the exercise test (35).

5- CONCLUSION

Asthma affects ventricular contractility in children. Although cardiac systolic function was found to be impaired in asthmatic patients, contrary to previous studies diastolic dysfunction wasn't observed in these patients even by Tissue Doppler Imaging, may be due to using inhaled corticosteroid. Future TDI studies with larger sample sizes or without using corticosteroid treatment might reveal important information on myocardial function patterns which their Interpretation should therefore be done with extreme caution, taking into account all the variables that might influence them.

6- ETHICS APPROVAL

This research was conducted according to the principles expressed in the Declaration of Helsinki and was approved by the Deputy of Research and Ethics Committee of Iran University of Medical Sciences (Iran) (ID-number: IR.IUMS.REC.1400.098).

7- CONFLICT OF INTEREST

None.

8- ACKNOWLEDGMENTS

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