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# Evaluation of Right Ventricular Function by Tissue Doppler Echocardiography in Asthmatic Children

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***Abstract***

***Background***

Asthma is the most chronic inflammatory disorder of the airways in children and asthmatic patients can experience cardiac dysfunction, pulmonary hypertension and finally cor pulmonale later in life. We aimed to investigate Right Ventricular (RV) functions in asthmatic children by conventional and tissue Doppler echocardiography (TDE).

***Materials and Methods***

Pulmonary function tests, conventional and TDE examinations were performed on 42 asthmatic and 42 age- and gender matched healthy controls subjects (n=42).

***Results***

Compared with healthy children the RV wall was statistically thicker among asthmatic patients (P= 0.01). Conventional echocardiography had not significant difference between cases and controls, but TDE had significant difference between these two groups. Peak $E^{'}$ velocity, $A^{'}$ velocity, $E^{'}/A^{'}$ ratio and $S^{'}$ in lateral and medial sites of tricuspid annulus valve, were significantly differ from control group in our patients (P<0.01). Isovolemic relaxation time and isovolemic contraction time were higher in asthmatic patients than the controls (P<0.01). Tie index or Myocardial performance index (MPI) had higher value in asthmatic patients (P<0.01). There was no difference in deceleration time between patients and cases (P=0.12).

***Conclusion***

Our study showed that although the conventional echocardiography and clinical finding were apparently normal in asthmatic children, TDE could showed subclinical dysfunction of the right ventricle in these patients. Our findings signify the diagnostic value of tissue Doppler-echocardiography superior to conventional echocardiography for the early evaluation, detection and monitoring of ventricular dysfunction among asthmatic patients.

***Key Words:*** Asthma, Children, Right ventricular function, Tissue Doppler Echocardiography.

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## 1- INTRODUCTION

Asthma which is the most chronic inflammatory disorder of the airways and most common chronic illness among children characterized by chronic inflammation and an obstruction of airflow, that may be partially or completely reversed during illness with or without therapy (1).

Inflammation in airway is associated with obstruction and hyper-responsiveness that leading to recurrent episodes of symptoms such as breathlessness, wheezing and cough. In different countries the global asthma prevalence ranges approximately from 1 to 18 % of the population. Recurrent exposure to hypoxemia in bronchial asthma, is one of the mechanisms with chronic and sustained inflammation in lungs (2). Narrowing of the pulmonary vasculature and consequently, pulmonary hypertension development, induced by pulmonary vasoconstriction due to releasing of various cytokines and mediators (3).

For the occurrence of cardiac dysfunction in asthmatic patients there are many explanations. Pulmonary hypertension leading to right heart dilation, ventricular hypertrophy and consequently impaired cardiac function, that known as cor-pulmonale in literature (4). Blood viscosity from polycythemia secondary to chronic hypoxia can increase Right ventricular (RV) afterload and pulmonary hypertension. RV dysfunction approximately depends on the degree of RV hypertrophy, RV afterload and pulmonary resistance. In pulmonary hypertension one of the most important prognostic factors is RV dysfunction (4).

For evaluation and assessment of ventricular function although many noninvasive and invasive parameters such as radionuclide ventriculography, Magnetic resonance imaging (MRI) and standard echocardiography are available, right ventricular function because of its position at the back of the sternum leads to poor image quality, and it remains difficult and challenging to quantify (5).

Furthermore to its position, the RV cavity has a specific anatomy and geometry than the LV, and RV function depends on another conditions, such as preload, afterload, and Left Ventricular (LV) function. Radionuclide ventriculography and MRI had their specific limitation for cardiac evaluation. For cardiac function evaluation echocardiography is a bedside, safe, and widely available technique in all centers. Echocardiographic modalities such as M-mode, two-dimensional, echo Doppler, and tissue Doppler imaging (TDI) are used in many systemic disease (6, 7). For the routine assessment of right ventricular function by two-dimensional echocardiography, it had difficulties due to its irregular shape and lung hyperinflation. Tissue Doppler echocardiography (TDE) is a new technique for quantitative measurement of regional myocardial velocities and intervals of systole and diastole (8).

Even when the gray-scale image is suboptimal, accurate and reproducible tracings can be obtained by TDE. TDE may be more sensitive than conventional echocardiography for detecting subclinical right ventricular abnormalities because of quantitative measures of regional function (9, 10).

Cor pulmonale could be experienced in patients with severe asthma during in their life gradually. Reports of echocardiographic examinations and cardiac function in children with asthma are scarcely available. Therefore, the purpose of this study was to assess the right heart function via echocardiography and TDE in children with bronchial asthma and to compare the data with those of a sample of normal children.

## 2- MATERIALS AND METHODS

This case-control study was conducted in the Pediatric department of Emam Hosein pediatric and research center during the period from Aug 2015 to Aug 2016. We studied 42 outpatients pediatric ages 5–15 years (24 [57.2%] male and 18 [42.8%] female), selected randomly from those with a proper diagnosis of bronchial asthma, and 42 healthy subjects. Inclusion criteria include:

- All patients meeting the criteria for bronchial asthma and aged between 5-15 years old (1).
- At least 4 weeks after last asthmatic attack,
- Had not any chronic disease such as gastroesophageal reflux, allergic rhinitis, upper respiratory infection, lung pathology and other heart disease,
- Had not received any corticosteroides during the last 4 weeks and 5 and
- -Body Mass Index (BMI) < 95%.

Complete physical examinations were performed by the physician in clinic. All of the patients and the controls underwent pulmonary function tests using spirometry forced expiratory volume 1 (FEV1), forced vital capacity (FVC), the ratio of FEV1 to FVC, and peak expiratory flow (PEF).

The control group included 42 healthy children selected from other healthy pediatric subjects from our center and properly matched with the study group in age, gender, and BMI, because obese subjects had diastolic changes correlate and progress with the degree of obesity (10). All the control subjects were free of any reactive airway disease or other pathologic lung disease and had normal pulmonary function test at rest and after standard 15 min of exercise. The protocol was approved by the local Research Ethics Committee at Esfahan University of Medical Sciences, and all parents gave informed consent. Through a questionnaire interview all the children included in this study (cases and control subjects) were subjected to full history-taking including data regarding age, gender, birth history, any family history of allergic diseases or asthma, severity of asthmatic attacks, predisposing factors, and drug using during and between asthma attacks. In all children body height, body weight, BMI, heart rate, respiratory rate, and blood pressure (BP) were recorded.

A clinical diagnosis of asthma, as suggested by episodic symptoms of airflow obstruction or airway hyper-responsiveness, for example, episodic cough, wheezing, breathlessness, and chest tightness responding to long-term asthma treatment as well as reversible airflow obstruction of at least 12 % of predicted forced expiratory volume in one second after use of a short-acting beta 2-agonist.

Conventional echocardiography was performed by a single experienced pediatric cardiologist, who was blinded to the patient's respiratory status and using with a Vivid 3 (General Electric Medical Systems, Milwaukee, WI) and 3- and 7-mHz transducers and simultaneous electrocardiogram (ECG) and phonocardiogram recording. The measurements of at least three cardiac cycles were averaged in sinus rhythm. End-systolic and end-diastolic dimensions of the left ventricle, interventricular septum, anterior wall thickness, and end-diastolic dimension of the right ventricle were measured at the parasternal long axis view. Fractional shortening (FS) was calculated (LV diastolic internal dimension- LV systolic internal dimensions/ LV diastolic internal dimension) at the papillary muscle in parasternal long axis view. With the pulse-wave Doppler sample volume placed at the tip of the tricuspid valve filling velocity was recorded from the apical four-chamber view during diastole. The peak velocity early diastole (E), peak velocity late

diastole (A), and deceleration time (DT) of the early diastolic velocity were measured in apical four chamber view. The ratios of E to A were calculated for tricuspid valve. Using TDE peak systolic (S') and early and late diastolic velocities (E' and A') were measured from the apical four-chamber view with the pulsed-wave Doppler sample volume placed at the lateral tricuspid annulus and interventricular septum and the ratio of early to late diastolic annular velocities were calculated. Isovolumetric relaxation time (IVRT) from the end of the S-wave to the beginning of E-wave, isovolumic contraction time (IVCT), from the end of tricuspid flow to the beginning of pulmonary flow or from the beginning of the first positive deflection after the Q-wave to the onset of the S-wave, and ejection time (ET) beginning to the end of the S-wave were measured and myocardial performance index (MPI), was calculated (IVRT+IVCT/ET). At least a mean of 3 clearest successive cycles was used for calculations.

### 2-1. Statistical Analysis

Quantitative data are expressed as mean ± standard deviation [SD] and $P<0.05$ was considered significant. 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. Pearson's correlation analysis was used to estimate correlations between pulmonary function tests and echocardiographic parameters. The collected data were analyzed using SPSS version 18.0 software (SPSS, Chicago, IL, USA).

## 3- RESULTS

The present study enrolled 42 asthmatic children (24 boys and 18 girls) who had a diagnosis of bronchial asthma with a mean age of 9.4 ± 2.1 years and matched with age and gender of healthy subjects. The characteristics of the patients, age and gender matched of healthy subjects are shown in **Table.1**. Echocardiographic findings are listed in **Table.2**. In patients and controls the mean height, weight, BMI, heart rate, systolic and diastolic blood pressure did not differ significantly ($P>0.05$). Among our patients the RV wall was significantly thicker than the healthy children ($P=0.01$). Conventional finding in echocardiography such as E and A velocity, E/A ratio at tricuspid valve, RV diameter, EF and fractional shortening (FS) did not differ significant between patients and controls ($P>0.05$).

Tissue Doppler study for diastolic function showed that peak E' velocity and peak A' velocity were significantly differ than the controls ($P<0.01$), and lower in these patients. The E'/A' ratio of the lateral tricuspid annulus and interventricular septum were significantly differ and higher among the cases than the controls, respectively ($P<0.05$). S' velocity at lateral tricuspid annulus and interventricular septum were significantly lower in patients than controls ($P<0.05$). The mean MPI or Tie-index for the right ventricle showed higher values in patients compares to controls and differ significantly ($P< 0.01$), and this showed that sum of IVCT and IVRT was greater in patients than the controls. There was no significant differ between DT in patients and cases ($P=0.12$). The spirometry values are shown in **Table.3**.

Pulmonary function tests were done for patient and control groups and PEF, FEV1, FVC, FEV1/FVC correlated with cardiac parameters. There were no differences between the asthmatic and control group. In correlation analysis, FEV1 was correlated with IVRT ($P= 0.01$ and $r=0.365$) and ET-MV ($P = 0.01$ and $r=0.345$) positively. PEF was negatively correlated with RVWI ($P = 0.01$and $r= -0.315$) and LVWI ($P = 0.01$ and $r= -0.265$), negatively.

**Table 1** Comparison (mean ± SD) of clinical characteristics

| Variables | Cases (42) | Controls (42) | P-value |
|---|---|---|---|
| Age (years) | 9.4 ± 2.1 | 9.7 ± 2.1 | - |
| Gender | | | |
| Male | 24 | 26 | - |
| Female | 18 | 16 | - |
| Height (cm) | 130 ± 12.4 | 132± 13.2 | 0.43 |
| Body weight (kg) | 29± 8.6 | 30± 7.9 | 0.54 |
| Body Mass Index BMI ($Kg/M^2$) | 20.18 ± 1.87 | 20.32± 2.07 | 0.67 |
| Heart rate (beat/min) | 85.48 ± 11.23 | 84.40 ± 9.82 | 0.91 |
| Respiratory rate (breath/min) | 19.2 ± 2.7 | 18.7± 2.5 | 0.85 |
| Blood Pressure (mmHg) | | | |
| Systolic | 107.44± 7.82 | 109.54 ± 8.22 | 0.42 |
| Diastolic | 61.15 ± 6.67 | 63.24 ± 7.24 | 0.38 |

SD: Standard deviation.

**Table-2:** Echocardiographic finding (Mean ± SD)

| Parameters | Cases | Controls | P-value |
|---|---|---|---|
| Conventional Echo | | | |
| Tricuspid | | | |
| E velocity (cm/s) | 106.5 ± 22.5 | 101.1 ± 22.1 | 0.67 |
| A velocity (cm/s) | 62.7 ± 26.2 | 63.2± 25.7 | 0.88 |
| E/A ratio | 1.7± 0.4 | 1.6± 0.5 | 0.15 |
| Free RV wall thickness (mm) | 4.7± 1.6 | 3.6± 1.4 | 0.01 |
| RV diameter (mm) | 17.4 ± 9.4 | 17.2±9.1 | 0.25 |
| TDE of RV at tricuspid | | | |
| Lateral wall | | | |
| E' velocity (cm/s) | 12.2±1.7 | 15.7±2.1 | 0.01 |
| A' velocity (cm/s) | 6.1±0.7 | 10.4±0.8 | 0.01 |
| E'/A' ratio | 2.0±0.48 | 1.50±0.39 | 0.01 |
| S' | 9.2±1.2 | 11.2±1.4 | 0.01 |
| Septal wall | | | |
| E' velocity (cm/s) | 12.8±1.7 | 15.3±1.9 | 0.01 |
| A' velocity (cm/s) | 6.2±0.6 | 10.6±0.7 | 0.01 |
| E'/A' ratio | 2.06±0.37 | 1.43±0.31 | 0.01 |
| S' | 9.3±1.3 | 11.4±1.7 | 0.01 |
| DT (ms) | 135.6 ± 34.0 | 128.4± 24.0 | 0.12 |
| Tie-index [MPI (%)] | 54.2%± 7.3 | 45%± 6.2 | 0.01 |
| IVRT | 69.7 ± 9.2 | 54.1 ± 7.7 | 0.01 |
| IVCT | 68.5 ± 9.8 | 51.4±9.1 | 0.01 |
| LV-EF (%) | 68.5± 9.3 | 69.2± 8.9 | 0.35 |
| LV-FS (%) | *38.9± 4.2* | 40.1 ± 3.2 | 0.42 |

A: peak velocity during late diastole; E: peak velocity during early diastole; A': Annular peak velocity during late diastole; E': Annular peak velocity during early diastole; S': Annular peak velocity during systole; DT: deceleration time; MS: millisecond; MPI: Myocardial performance index; IVRT: isovolumetric relaxation time; IVCT: isovolumetric contraction time; LVEF: left ventricular ejection fraction; LV-FS: left ventricular fractional shortening.

**Table-3:** Spirometry findings (Mean ± SD)

| Parameters | Cases | Controls | P-value |
|---|---|---|---|
| PEF | 82.05 ± 8.7 | 90.8 ± 9.1 | 0.25 |
| FEV1 | 78.8 ± 10.2 | 88.2 ± 9.6 | 0.003 |
| FVC | 90.1 ±7.5 | 93.2+8.4 | 0.22 |
| FEV1/FVC | 80.2 ± 9.7 | 89.4± 10.5 | 0.022 |

SD: Standard deviation.

## 4- DISCUSSION

In current study we aimed to assess RV function in controlled asthmatic by conventional and TDE exam. Chronic hypoxemia and sustained inflammation, could be leads to pulmonary vasoconstriction and consequently, pulmonary hypertension may develop in asthmatic patients, which could then lead to right ventricular hypertrophy and enlargement (4, 11). In patients with moderate to severe asthma echocardiographic studies showed evidence of RV and LV diastolic dysfunction (12, 13).

Researchers showed that in asthmatic patients RV diastolic dysfunction to be the earliest cardiac hemodynamic change and this change is proposed to depend on pulmonary resistance and RV hypertrophy. We guess that TDE could be used for investigate of negative impact of asthma on right ventricle function in early life before other gross sings. Our patients were 5-15 years old, because of their best cooperation among pediatric field and had the highest rate of asthma in all age group (14). Studies showed that the RV wall was thicker among the asthmatic patients and other RV echocardiographic dimensions did not differ significantly from those of the control subjects (15, 16). Improvement in RV diastolic functions were observed in asthmatic patients after treatment and decrease in pulmonary hypertension and RV afterload. Our results confirms these results and in current study similar to their studies except RV wall thickness other parameters in conventional echocardiographic of asthmatic patients such as EF, FS, E and A velocities were similar to controls. These studies support that despite development of RV hypertrophy in asthmatic children, conventional echocardiography is not sufficient to assess RV functions in asthmatic patients. This insufficiency may result from the complex geometry of RV, its retrosternal location hyperinflation of the lungs in patients with asthmatic patients. Even when image quality is suboptimal TDE allows assessment of ventricular systole and diastole function and regional myocardial velocities (17).

Therefore, TDE for detecting subclinical RV abnormalities may be more sensitive.

Tayyareci et al. showed that the parameters of TDE-determined RV dysfunction, were complementary conventional echocardiography and had correlated with pulmonary hypertension and respiratory function tests in asthmatic patients (18). They showed that TDE to be useful for RV functions assessment in subclinical pulmonary hypertension. $E^{'}$, $A^{'}$ and $S^{'}$ were significantly lower in Shedeed study and $E^{'}/A^{'}$ ratio, IVRT and IVCT were significantly greater than normal subjects in their study by using TDE (15). They showed that TDE parameters can determine RV dysfunction at early stages in asthmatic patients. In our study similarly, $E^{'}$, $A^{'}$, $E^{'}/A'$, and IVRT of lateral tricuspid annulus and interventricular septum was significantly different between patients and controls and showed that asthmatic children had an decreased relaxation pattern of the RV and

a consequently impaired RV diastolic function. Also, in our study the patients had significantly lower systolic velocities in the RV at septal and interventricular septum S' than the controls that similar to Soad study (19). Myocardial performance index (MPI) is a useful and simple clinical index that is reported to be independent of heart rate and ventricular geometry for evaluation of global ventricular function. For this reason, MPI is used to evaluate the cardiac effects of multiple systemic disease (7, 20).

In asthmatic patients, longer IVRT and MPI of the right ventricle, as well as subclinical RV dysfunction, were shown using TDE in early life and were greater than normal subjects (21). In our study IVRT and MPI were greater than normal subjects and these finding suggest ventricular dysfunction in these patients and therefore, subclinical RV diastolic dysfunction was shown using diastolic myocardial velocities and MPI in these children. This means that asthmatic patients have right ventricular dysfunction even had conventional normal parameters echocardiography.

### 4-1. Limitations of the study

Our most study limitation was the small number of patients and larger group of patient for other studies is suggested.

## 5- CONCLUSION

This study showed that assessment of ventricular functions using TDE study demonstrated subclinical right ventricular dysfunction although the conventional echocardiographic findings of asthmatic children were normal. These findings signify the diagnostic value of TDE in the early evaluation, detection and monitoring of asthmatic patients.

## 6- CONFLICT OF INTEREST

The authors had not any financial or personal relationships with other people or organizations during the study. So there was no conflict of interests in this article.

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