Doppler Echocardiographic Evaluation Of Ventricular Function In Patients With Bronchial Asthma

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Abstract:
Cardiac involvement in bronchial asthma (BA) has been reported previously. However, evaluation of ventricular function in this disease by the use of recently proposed Doppler echocardiographic methods has not been reported before. Therefore, the aim of this study was to evaluate ventricular function by measurement of myocardial performance index (MPI) and transmitral flow propagation velocity (TFPV). Sixty patients with bronchial asthma and 20 control subjects (mean ages 6-16 and 8-14 years, respectively) participated in this study. Systolic function was assessed by subjective evaluation of wall motion for both ventricles and by fractional shortening for the left ventricle (LV). LV diastolic function was evaluated by standard pulsed-wave Doppler echocardiography, MPI and TFPV. Right ventricular (RV) function was evaluated by MPI. No subject had signs or symptoms of clinically overt heart failure. Systolic function was normal in all subjects. Among the echocardiographic indices of LV diastolic function the peak E velocity, E velocity/A velocity ratio, isovolumetric relaxation time, MPI and TFPV in the BA group were significantly different from those of the controls (P <0.05). However, we did not observe a significant difference in RV echocardiographic indices between the two groups. Our results show that there is LV diastolic dysfunction in patients with bronchial asthma.

Abbreviations: BA: bronchial asthma, MPI: myocardial performance index, TFPV: transmitral flow propagation velocity, LV: left ventricle, RV: Right ventricle.

Introduction:
Bronchial Asthma (BA) is an inflammatory disease with edema, bronchial constriction, and mucous plugging. Dramatic worldwide variations in asthma prevalence have been found with the highest rates in the United Kingdom, Australia, and New Zealand, and the lowest prevalence in Eastern Europe, China, and India.1-3 About 10% of Egyptian children have asthma and its prevalence, morbidity, and mortality have been increasing especially in children < 12 years of age.4 Until recently, left ventricular (LV) diastolic function has generally been evaluated by pulsed-Doppler echocardiography of LV inflow. Although easily achieved, the method has several drawbacks: it affected by changes in preload and afterload; tachycardia or first degree atrioventricular block may result in fusion of the E and A velocities; and pseudonormalization is another limiting factor, which complicates the diagnosis of diastolic function.
Recently myocardial performance index (MPI) and transmitral flow propagation velocity (TFPV) have been suggested for the evaluation of ventricular function. MPI is calculated from the pulsed Doppler recordings of ventricular inlet and outlet velocities and thus combines both systolic and diastolic ventricular performance. It reflects global ventricular function and is less affected by localized wall motion abnormalities. It has been shown to be independent of changes in preload and afterload in the assessment of right ventricular (RV) myocardial performance.5,6 In their study of 26 patients with primary pulmonary hypertension and 37 age-matched controls, Tei et al.7 reported that the index was not significantly affected by heart rate, tricuspid regurgitation, right ventricular pressure or right ventricular dilatation. TFPV is obtained from color Doppler M-mode echocardiography and is used to assess LV diastolic function. This technique has been shown to be relatively independent of preload in patients with hypertrophic cardiomyopathy,5 dilated cardiomyopathy 9,10 and pulmonary hypertension.11,12 In a recent study, the Peak E-velocity/TFPV ratio was found the best estimate of pulmonary wedge pressure.13 To our knowledge, ventricular performance in bronchial asthma has not been evaluated by measurements of MPI or TFPV in the past. Therefore, we evaluated ventricular function in patients with BA by standard pulsed-wave Doppler echocardiography and also by MPI and TFPV.

Subjects and Methods:
Sixty patients who met the criteria for asthma 14,15 including recurrent episodes of wheezing,
troublesome cough at night, or cough, wheeze, or chest tightness after exercise or exposure to airborne allergens or pollutants, were recruited from outpatient clinics of pediatric and chest departments of El-Minia University Hospital. Seven patients were boys, and nine patients were girls. The age of the patients ranged from 6 to 16 years, with a mean age ± SD of 12.3 ± 3.0 years. The severity of asthma, as determined by the clinical symptoms and PEFR, was mild to moderately persistent.16

The 20 healthy volunteer children included 8 boys and 12 girls, ranging in age from 8 to 14 years with a mean age of 9.8 ± 3.2 years. All healthy subjects had no history of rhinitis, eczema, or spontaneous wheezing, and were not receiving any medication. Study patients underwent a complete physical examination. None of them had respiratory tract infections, diabetes mellitus, systemic hypertension, congenital cardiac malformation, arrhythmia, heart failure or valvular heart disease. Written informed consent was obtained from all of the subjects before the study commenced.

Echocardiographic examination was performed using an HP-SONOS 1000 ultrasonic imaging machine (Hewlett-Packard, Inc., USA) with 7.5 MHz phased-array transducer and a color-coded Doppler screen. Real time 2D, M-mode, colored and Doppler study was done for all cases. Spectral Doppler tracings were recorded and stored on magnetic optical disks for later analyses. Both the echocardiographic examination and the analyses of recordings were made blinded to the clinical diagnoses. LV, left atrial and aortic root dimensions were measured as previously recommended.17

For pulsed Doppler recordings of ventricular inflow, the sample volume was placed in the tips of the mitral and tricuspid leaflets. MPI was calculated as the sum of isovolumetric contraction and isovolumetric relaxation time divided by the LV ejection time. It can be calculated easily by a simple formula: (a-b)/b (18). On pulsed Doppler spectrum of the ventricular inflow, the time interval "a" from the cessation to the onset of ventricular inflow was considered as the sum of isovolumetric relaxation time (figure 1). The ventricular ejection time "b" was the duration of ventricular outflow velocity profile (figure 2). The isovolumetric relaxation time, isovolumetric contraction time, peak E velocity, peak A velocity and the deceleration time of the E wave were also measured.

TFPV was obtained by color Doppler M-mode echocardiography from the apical four chamber view as described by Garcia et al.19 The slope of the first aliasing velocity during early filling, from the mitral valve plane to 4 cm distally into the LV cavity, was measured and the peak E velocity/TFPV was calculated. Electrocardiographic monitoring was performed throughout the entire echocardiographic examination.

To decrease the effect of beat-to-beat variation, an averaged of the analyses of three cardiac cycles was used for each echocardiographic parameter. Doppler recordings were made at the end of expiration to minimize the effects of respiration. The recordings of 10 randomly selected subjects were reanalyzed on a different day to determine the interobserver variability. These recordings were also analyzed by another cardiologist to determine the interobserver variability.

Statistical Analyses:
All results were expressed as mean ± SD. Comparison of the mean values between the two groups was performed with Student's t-test. A P value < 0.05 was considered significant.

Results:
The clinical features of the studied subjects are given in table I. There were no significant differences in age, heart rate, systolic and diastolic blood pressures between bronchial asthma patients and controls. Subjective evaluation of the wall motion of both ventricles, and the fractional shortening of LV was normal (> 35%) in all subjects. The LV, left atrial, and
aortic root dimensions were all within normal limits and not significantly different between the two groups. Non of the subjects had LV hypertrophy. The thickness of both the interventricular septum and the posterior wall was < 10 mm in all subjects.

Table I: Characteristics of Study Subjects

<table>
<thead>
<tr>
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<th>Study Group (n = 16)</th>
<th>Control Group (n = 20)</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>12.3 ± 3.0</td>
<td>9.8 ± 3.2</td>
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<tr>
<td>Sex (male/female)</td>
<td>7/9</td>
<td>8/12</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>149.6 ± 17.5</td>
<td>130.5 ± 27.9</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>80 ± 8</td>
<td>95 ± 6</td>
</tr>
<tr>
<td>Systolic BP (mm Hg)</td>
<td>100 ± 8</td>
<td>95 ± 7</td>
</tr>
<tr>
<td>Diastolic BP (mm Hg)</td>
<td>85 ± 6</td>
<td>56 ± 6</td>
</tr>
<tr>
<td>FEV1, % Predicted</td>
<td>85.9 ± 9.2</td>
<td>90.1 ± 7.5</td>
</tr>
<tr>
<td>PaO2 Predicted (mmHg)</td>
<td>54 ± 12</td>
<td>92 ± 5</td>
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</table>

P > 0.05 for all of the above variables

Among the pulsed-wave Doppler indices in left ventricular diastolic function, we observed significant differences in the peak E-velocity, peak E velocity/peak A velocity ratio and isovolumetric relaxation time between the two groups (P < 0.05). Mean LV MPI in the bronchial asthma group (0.42 ± 0.11) was also significantly higher than that of the controls (0.38 ± 0.11, P < 0.05). The normal value for LV MPI was formerly reported a 0.039 ± 0.05. Our data (0.42 ± 0.11) are clearly out of both normal ranges. On the other hand, there were no significant differences in the mean value of peak A velocity, deceleration time and isovolumetric contraction time between bronchial asthma patients and controls (table II).

Table II: Echocardiographic indices in left ventricular functions

<table>
<thead>
<tr>
<th></th>
<th>Study Group (n = 16)</th>
<th>Control Group (n = 20)</th>
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<tbody>
<tr>
<td>E velocity (cm/s)</td>
<td>59 ± 13 *</td>
<td>72 ± 16</td>
</tr>
<tr>
<td>A velocity (cm/s)</td>
<td>70 ± 18</td>
<td>63 ± 14</td>
</tr>
<tr>
<td>E/A velocity ratio</td>
<td>0.8 ± 2.7 *</td>
<td>1.2 ± 0.3</td>
</tr>
<tr>
<td>Isovolumetric relaxation time (ms)</td>
<td>72 ± 23 *</td>
<td>54 ± 24</td>
</tr>
<tr>
<td>Deceleration time (ms)</td>
<td>160 ± 42</td>
<td>145 ± 32</td>
</tr>
<tr>
<td>Isovolumetric contraction time (ms)</td>
<td>34 ± 12</td>
<td>36 ± 13</td>
</tr>
<tr>
<td>Ejection time (ms)</td>
<td>262 ± 28</td>
<td>276 ± 28</td>
</tr>
<tr>
<td>Myocardial performance index (MPI)</td>
<td>0.42 ± 0.11 *</td>
<td>0.38 ± 0.11</td>
</tr>
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Color Doppler M-mode Echocardiography:

- TFPV (cm/sec) | 35 ± 11 | 42 ± 9
- E velocity/TFPV | 1.8 ± 0.8 | 1.8 ± 0.6

TFPV Transmitral flow propagation velocity, *P < 0.05

 tropical asthma is not a rare disease and the relationship between right ventricular and left ventricular function in this setting remains uncertain. Physical examination, electrocardiogram, and chest radiographs are unreliable in making the diagnosis of ventricular diastolic dysfunction in most individuals, and invasive measurements of cardiac pressures, rates of ventricular relaxation, and ventricular compliance are costly, clinically impracticable as well as software analysis programs. Because the two ventricles influence each other's performance this study was designed to investigate the impact of bronchial asthma evaluate ventricular function.

Table III: Echocardiographic indices in right ventricular functions

<table>
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<tr>
<th></th>
<th>Study Group (n = 16)</th>
<th>Control Group (n = 20)</th>
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<tbody>
<tr>
<td>Isovolumetric relaxation time (ms)</td>
<td>38 ± 12</td>
<td>41 ± 14</td>
</tr>
<tr>
<td>Isovolumetric contraction time (ms)</td>
<td>36 ± 12</td>
<td>38 ± 12</td>
</tr>
<tr>
<td>Ejection time (ms)</td>
<td>280 ± 26</td>
<td>290 ± 31</td>
</tr>
<tr>
<td>Myocardial performance index</td>
<td>0.30 ± 0.12</td>
<td>0.26 ± 0.06</td>
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Discussion:

The cardiovascular status in patients with bronchial asthma has not been extensively studied and the relationship between right ventricular and left ventricular function in this setting remains uncertain. Physical examination, electrocardiogram, and chest radiographs are unreliable in making the diagnosis of ventricular diastolic dysfunction in most individuals, and invasive measurements of cardiac pressures, rates of ventricular relaxation, and ventricular compliance are costly, clinically impracticable as well as software analysis programs. Because the two ventricles influence each other's performance this study was designed to investigate the impact of bronchial asthma evaluate ventricular function.

The present study shows that LV MPI and TFPV can identify the presence of LV dysfunction in patients with bronchial asthma. Both methods of measurements are easily obtained and are not affected by ventricular geometry. Our findings are completely in concordance with the classic measurements of LV diastolic dysfunction, namely decreased E/A ratio and prolonged isovolumetric relaxation time.

Several mechanisms may be responsible for diastolic dysfunction in bronchial asthma. The first and most important factor is the significantly increased heart rate in the bronchial asthma group. Tachycardia shortened the diastolic filling period and atrial contraction may have occurred before the early filling was completed; the myocardial performance index will be higher than it would be if the heart rate were slower. This tachycardia may be due to multiple causes including hypoxemia or medications. Our patients all presented with a mild to moderate hypoxemia and bronchial asthma patients are known to show a more pronounced reaction to low blood oxygen content. Medications given to the bronchial asthma patients included B2-agonist, theophylline, or anticholinergic drugs, all potentially responsible for tachycardia. Color Doppler M-mode echocardiography showed a decreased transmitral flow propagation velocity (TFPV) of the bronchial asthma group. This decreased LV preload may have contributed to the acceleration of the heart rate. Reduced LV preload...
could be due to reduced venous return flow or to hypovolemia. Obstruction of the bronchi may have increased intrinsic positive end-expiratory pressure and limited the venous return blood flow. A recent study also showed that patients with obstructive pulmonary disease tended to be systemically vasodilated, depending on the severity of hypoxemia. Experimental research in healthy subjects submitted to long periods of altitude-induced hypoxia has shown a marked decrease in LV preload, owing to a reduction in their plasma volume. The mechanism might be the inhibition of sodium reabsorption in the renal tubules secondary to hypoxemia. Tachycardia, hypoxemia and reduced LV preload might contributed to the observation of LV diastolic dysfunction in our patients. Changes in the LV filling rate do not seem to be the consequence of a LV systolic dysfunction, because the parameters of LV systolic function were similar in both studied groups. This result is in agreement with previous findings in patients with bronchial asthma. Moreover, there was no evidence of LV hypertrophy in our bronchial asthma group, which might have explained LV filling abnormality. The absence of LV hypertrophy in our patients was probably due to the exclusion of patients with hypertension or cardiac failure. Few studies have been done on right ventricular function in bronchial asthma and its role has been probably been underestimated. Eniseera et al., reported that in patients with bronchial asthma, the degree of right ventricular dysfunction depends on right ventricular hypertrophy an total pulmonary resistance. Recently, Chicherina et al., in the largest study to date concluded that diastolic dysfunction of the right ventricle was the earliest hemodynamic changes in bronchial asthma and left ventricular dysfunction appears to be related to right ventricular dysfunction perhaps through ventricular independence. Right ventricular dysfunction is more common in systemic hypertension, pulmonary hypertension, chronic core pulmonary, heart failure, and cardiomyopathy. In our study, our results showed that RV MPI is preserved despite an abnormal LV MPI. This was in agreement with Alpaslan et al. There was no clear explanation for this and the present study was not designed to elucidate it. Young age of the studied bronchial asthma group is a limitation of this study. The RV MPI was reported to be a powerful echocardiographic parameter in differentiating patients with primary pulmonary hypertension from the healthy subject. The short duration of symptoms, combined with the absence of clinical/echocardiographic evidence for chronic lung disease, may also explain our failure to observe a significant difference in the echocardiographic parameters of RV function. Further studies including older age groups may give diverse results concerning the RV MPI.

Conclusion:
This study shows that LV diastolic function is impaired in patients with bronchial asthma. MPI and TFPV confirm the classic measurements of pulsed-wave Doppler LV inflow and suggest an early stage of LV diastolic dysfunction in the course of the disease.

References:
9. Moller JE, Poulsen SH, Sondergaard E, Egstrup K. Preload dependence of color M-mode Doppler flow propagation velocity in controls and in patients with left