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Evaluation of cardiac function in pediatric patients with mild to moderate bronchial asthma in the era of cardiac strain imaging

Gaser Abdelmohsen MD[1] | Hossam Mohamed MD[1] | Mona Mohsen MD[2] | Osama Abdelaziz MD[1] | Doaa Ahmed MSc[2] | Mohamed Abdelsalam MD[3] | Ahmed Dohain MD[1]

[1]Pediatric Cardiology Division, Department of Pediatrics, Cairo University, Cairo, Egypt

[2]Pediatric Pulmonology Division, Department of Pediatrics, Cairo University, Cairo, Egypt

[3]Cardiology Department, Benha University, Benha, Egypt

Correspondence
Gaser Abdelmohsen, MD, Pediatric Cardiology Division, Department of Pediatrics, Faculty of Medicine, Specialized Pediatric Hospital, Cairo University, Kasr Al Aini St, Cairo 11562, Egypt.
Email: gaser_abdelmohsen81@yahoo.com

Abstract

Objective: Bronchial asthma is a common chronic inflammatory airway disease, which may be associated with pulmonary hypertension and cardiac dysfunction. The aim of this study was to evaluate the ability of 2D-speckle tracking echocardiography (2D-STE) and tissue doppler imaging (TDI) to detect subtle cardiac dysfunction in pediatric patients with mild to moderate bronchial asthma.

Methodology: The study included 30 children with mild to moderate bronchial asthma and 27 age-matched healthy controls. Both groups underwent pulmonary function tests, TDI and 2D-STE. Myocardial performance index (MPI), S′, E′, A′ velocities, global strain of left ventricle (LV), right ventricle (RV), and right atrium (RA) were measured.

Results: RV diastolic function was impaired in the patient group, as the tricuspid E′ velocity was significantly lower in the patients when compared with the controls (16 [14-17] vs 16 [17-19] cm/s, $P = .044$), while the RV-MPI was significantly higher in patients when compared to controls (0.30 [0.27-0.36] vs 0.30 [0.30-0.30], $P = .001$). The global RV longitudinal strain, RA strain, and LV strain did not show significant differences between the test and the control groups. RV systolic parameters and LV systolic and diastolic parameters did not differ significantly between the two groups.

Conclusion: Pediatric patients with mild to moderate bronchial asthma may have early RV diastolic dysfunction with preserved other cardiac functions.

KEYWORDS

left ventricle strain, pediatric bronchial asthma, right atrial strain, right ventricle strain, speckle tracking echocardiography

Abbreviations: 2D-STE, 2 dimensional speckle tracking echocardiography; BPM, beat per minute; BSA, body surface area; CW, continuous wave; ECG, electrocardiogram; EF, ejection fraction; ET, ejection time; FEV1, forced expiratory volume in 1 second; FS, fraction of shortening; FVC, forced vital capacity; GAS, global atrial strain; GCS, global circumferential strain; GE, general electric; GLS, global longitudinal strain; GRS, global radial strain; GS, global strain; ICS, inhaled corticosteroids; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time; LV, left ventricle; LVEDD, left ventricle end-diastolic dimension; LVESD, left ventricle end-systolic dimension; MPI, myocardial performance index; PAP, pulmonary artery pressure; PEF, peak expiratory flow; PEP, pre-ejection period; PRN, as needed; PVR, pulmonary vascular resistance; PVTI, pulmonary velocity time integral; PW, pulsed wave; RA, right atrium; ROI, region of interest; RV, right ventricle; RVAWD, right ventricle anterior wall diameter; RVDD, right ventricle diastolic dimension; RVOT, right ventricle outflow tract; SABA, short acting β agonists; TAPSE, tricuspid annular peak systolic excursion; TDI, tissue Doppler imaging; TRV, tricuspid regurgitation velocity.

1 | INTRODUCTION

Bronchial asthma is a common chronic inflammatory airway disorder in the pediatric population. It places a significant burden on patients, families, and health care providers, especially during periods of exacerbation that may be serious enough to require hospital admission.[1,2]

Bronchial asthma may be complicated by an increase in pulmonary vascular resistance, which consequently leads to secondary pulmonary hypertension and right ventricle (RV) dysfunction, caused by several mechanisms. The release of inflammatory mediators due to chronic inflammation of the airway may cause pulmonary vasoconstriction and distortion of pulmonary vasculature.[3-7] The left ventricle (LV) could be affected secondary to RV involvement due to ventricular interdependence.[8]

For decades, conventional echocardiography was widely used for evaluation of cardiac function, but unfortunately, it is limited by the poor echocardiographic windows associated with lung hyperinflation. In addition, the complex anatomy of the right ventricle prevents its functional assessment by any geometrical assumption. Tissue doppler imaging (TDI) is a relatively new modality used for quantitative measurement of regional myocardial velocities and intervals, especially if the 2D images are suboptimal. It might be more sensitive than conventional echocardiography for detecting subtle ventricular dysfunction. This technique is, however, angle-dependent and is affected by translational heart movements.[9] 2D speckle tracking echocardiography (2D-STE) has overcome these limitations and is therefore considered to be superior to TDI in evaluating myocardial function.[8,10,11] The main aim of the present study was to evaluate the ability of 2D-STE and TDI besides the conventional echocardiography for up detecting cardiac dysfunction in children with mild to moderate bronchial asthma.

2 | MATERIALS AND METHODS

The present study was a prospective study conducted among 33 pediatric patients with mild to moderate bronchial asthma (the patient group) and 28 controls (the control group). The control group was composed of similarly aged healthy children, who did not significantly differ from the patient group regarding weight, height, body surface area (BSA), or sex distribution. The control group was recruited from the outpatient pediatric clinic and comprised of children presented with minor complains like headache, sore throat or children came for routine evaluation before participation in sport activities. The diagnosis and classification of severity of asthma were established according to the National Asthma Education and Prevention Program, Expert Panel Report-3.[12] Table 1 summarizes the demographic features of each group. Patients with severe asthma or having a congenital/acquired heart disease, who had a systemic disease with impact on cardiac or respiratory functions (eg, obesity, obstructive sleep apnea, collagen vascular disease), who were on chemotherapy or cardiac medications, or with suboptimal echocardiographic views were excluded from the study. Formal written consents were taken obtained from the parents, and the study was approved by the ethical committee of the Faculty of Medicine, Cairo University. Patient and control groups underwent *pulmonary function tests* and the following parameters were obtained: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), forced expiratory volume in 1 second/forced vital capacity ratio (FEV1/FVC) and peak expiratory flow (PEF). Values measured were (% of the predicted values). Echocardiography was performed for both groups using General Electric (GE, Vivid-7) system with a probe 3 or 5 MHz multifrequency transducer according to each patient's age. The echocardiographic examination was done between episodes of acute exacerbation to avoid poor echocardiographic windows associated with lung hyperinflation. Patients with suboptimal 2D echocardiographic windows preventing adequate speckle tracking and those patients with an inadequate tracing of their tricuspid regurgitation jet were excluded from further analysis. Accordingly, one patient was excluded due to suboptimal 2D images, and three participants (Two patients and one control) were excluded from further analysis due to the inadequate tracing of TR jet velocity. After exclusion of these four participants, the total number of participants was 30 patients and 27 controls.

The following modalities were used:

1. *M-mode: The left ventricle was assessed in a* parasternal long-axis view. The following M-Mode derived parameters were measured: LV ejection fraction (EF), LV fraction of shortening (FS), left ventricle end-diastolic dimension (LVEDD), left ventricle end-systolic dimension (LVESD), (right ventricle diastolic dimension (RVDD), and RV anterior wall diameter (RVAWD). The apical four-chamber view was obtained for measurement of the tricuspid annular peak systolic excursion (TAPSE).
2. Conventional Doppler:

a. Pulsed wave Doppler (PW):The mitral valve was viewed in an apical four-chamber view and the pulsed wave Doppler-derived peak early (E) and late (A) wave velocities were measured.For assessment of right ventricle outflow tract (RVOT), the parasternal short-axis view was used for measurement of acceleration time (AT), ejection time (ET), pre-ejection period (PEP), velocity-time interval (VTI) and PEP/ET. PEP was measured from the start of the QRS complex to the start of pulmonary ejection velocity, ET was measured from the start to the end of pulmonary ejection velocity, and AT was measured from the start to the peak of pulmonary ejection velocity.

b. Continuous wave (CW) Doppler:

Depending on the view that gives the best continuous Doppler tracing of tricuspid regurgitation (TR) jet, either the apical four chamber view, parasternal short axis view or the parasternal long axis inflow view was used. The pulmonary artery pressure (PAP) was measured according to the formula: $PAP = TRV^2 + RA$ pressure,[13] where TRV refers to the tricuspid regurgitation velocity, and RA

TABLE 1 Characteristics of studied groups

Parameters	Patients (n = 30)	Control (n = 27)	*P* value
Age, y	9.50 (8.00-11.00)	9.00 (8.00-11.00)	.728
Weight, kg	30.00 (27.75-35.50)	30.00 (26.00-37.00)	.512
Height, cm	133.50 (128.00-140.00)	131.00 (128.00-142.00)	.755
BSA, m^2	1.00 (0.92-1.18)	1.00 (0.95-1.22)	.474
Heart rate, BPM	86.00 (79.00-90.00)	80.00 (76.00-86.00)	.093
FVC (% predicted)	93.90 (87.90- 103.00)	103.00 (100.00-109.00)	.001*
FEV1 (% predicted)	94.50 (85.95-101.10)	105.10 (99.90-106.70)	<.0001*
FEV1/FVC (% predicted)	94.50 (85.92-100.05)	100.00 (98.00-102.40)	.007*
PEF (% predicted)	83.25 (79.98-86.12)	91.00 (89.00-95.80)	<.0001*
Sex, n (%)			.943
Male	12.00 (40.00)	12.00 (44.40)	
Female	18.00 (60.00)	15.00 (55.60)	
Severity, n (%)			
Mild	23.00 (76.70)		
Moderate	7.00 (23.30)		
Medications, n (%)			
Inhaled SABA (PRN)	23.00 (76.67)		
ICS (low dose)[a]	3.00 (10.00)		
ICS (moderate dose)[b]	4.00 (13.33)		
Family history of atopy, n (%)			
Positive	29.00 (96.70)		
Negative	1.00 (3.30)		

Abbreviations: BPM, beat per minute; BSA, body surface area; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; PEF, peak expiratory flow; PRN, Latin word "pro re nata", means as needed; SABA, short acting beta agonist.
[a]Patients were on both PRN SABA and low dose ICS (50 μg every 12 h).
[b]Patients were on both PRN SABA and moderate dose ICS (125 μg every 12 h).
*Statistically significant.

pressure refers to the right atrial pressure which assumed to be 5mm Hg for all participants.

3. *Pulmonary Vascular resistance (PVR):* PVR was evaluated by combining tricuspid regurgitation velocity (TRV) and velocity time integral of right ventricular out flow tract (VTI_{RVOT}), $PVR = TRV^2/VTI_{RVOT}$ according to Abbas et al.[14]
4. *Pulsed wave Tissue Doppler imaging (PW-TDI):* PW-TDI was assessed using the apical four chamber view. Care was taken to increase the frame rate to greater than 180 frames/second and to minimize the interrogation angle to the targeted ventricular wall to less than 15°. Four consecutive cardiac cycles were obtained and the mean value of each of the following parameters was calculated: Systolic (S′), diastolic (E′, A′, E′/A′ ratio) myocardial velocities at the basal segments of the lateral LV wall, septal wall, and RV free wall.[15] Myocardial performance index (MPI) was also measured for both the LV and the RV at the LV lateral wall and the RV lateral wall, respectively. MPI = (ICT + IRT)/ET, where ICT is the isovolumetric contraction time, IRT is the isovolumetric relaxation time, and ET is the ejection time.[16,17]
5. *2D speckle tracking echocardiography (2D-STE):* 2D images were obtained in the apical four chambers, apical long axis and apical two chambers views for evaluation of LV global longitudinal strain (GLS).

The parasternal short axis views at LV base, papillary muscles, and apex were used for evaluation of LV global circumferential strain (GCS) and global radial strain (GRS).

The global longitudinal strain of the RV was measured in the apical four-chamber view (Figure 1B). Right atrial (RA) strain was performed in the apical four-chamber view. Medium gain and a minimum region of interest (ROI) were applied to fit the evaluation of the RA strain. The reference point was adjusted at the onset of the P wave allowing measurement of the negative global atrial strain at maximal atrial contraction (negative GAS/pump function) and positive global atrial strain (positive GAS/conduit function, Figure 1A).

2D-STE was performed as previously described.[10,18-22] The frame rate of the obtained cine loops was adjusted between 60 and 90 frames/second. Care was taken to keep the heart rate in the same range in the stored loops. Good quality cine loops from three cardiac cycles were digitally saved, then exported to the Echo-PAC software (Echo PAC version 11, GE) for further STE offline analysis.

2.1 | Statistical analysis

SPSS Version 20 software (IBM, Armonk, New York) was used for Statistical analysis. The numerical data were expressed as median

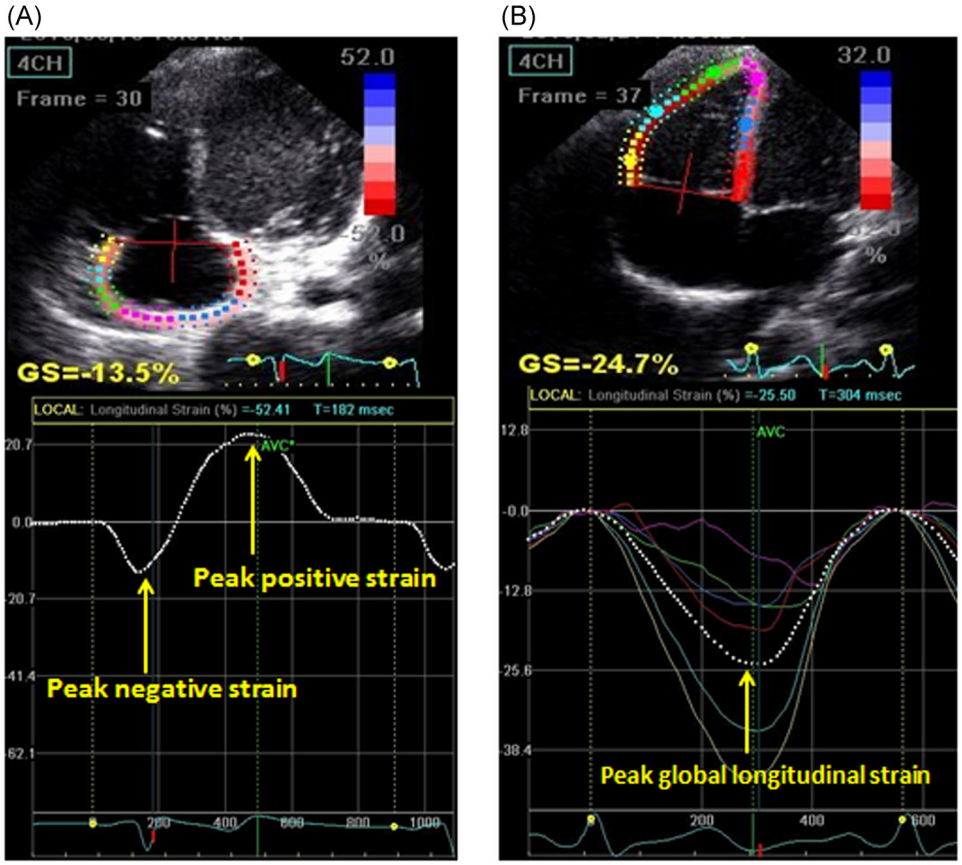

FIGURE 1 A, Evaluation of right atrial strain using 2D-speckle tracking echocardiography. B, Evaluation of right ventricle global longitudinal strain using 2D-speckle tracking echocardiography. GS, Global strain [Color figure can be viewed at wileyonlinelibrary.com]

and interquartile ranges (25th-75th percentiles) while the categorical data were expressed as numbers and percentages. Comparisons between the groups were calculated using nonparametric Mann-Whitney test for numerical data and χ^2 tests for categorical data. Correlation between variables was calculated using the Spearman correlation coefficient. Graphs were performed created using MedCalc for Windows software, version 15.0 (MedCalc Software, Ostend, Belgium). Statistical significance was considered to be present if $P < .05$.

3 | RESULTS

3.1 | Clinical data of the studied groups

The control group did not differ statistically significant from the patient group regarding the age, weight, height, body surface area (BSA) or sex distribution (Table 1). Twenty-three patients (76.7%) had mild asthma while seven patients (23.3%) had moderate asthma. Most of the patients (23 patients) were receiving inhaled short-acting β agonists (SABA) as needed (PRN), while seven patients were receiving inhaled corticosteroids beside PRN inhaled SABA. Positive family history of atopy was reported in 29 patients (>96%). FVC, FEV1, FEV1/FVC, and PEF were significantly lower in the patients' group (Table 1).

3.2 | Right heart and pulmonary vascular properties of the participants

3.2.1 | M-Mode RV dimensions

The patient group had RV dilatation rather than hypertrophy compared with the control group, since that the RV anterior wall diameter (RVAWD) did not differ significantly between patients and controls, while RVDD was significantly higher in the patients' group ($P < .01$, Table 2).

3.2.2 | RV systolic function

TAPSE, S′ velocity at the tricuspid annulus and global longitudinal strain of RV did not show significant differences between patient and control groups (Table 2).

3.2.3 | RV diastolic function

The tricuspid E′ velocity was significantly lower in patients compared with control ($P < .05$, Figure 2). In contrast, the myocardial

TABLE 2 Right heart parameters of studied groups

Parameters	Patients (n = 30)	Control (n = 27)	*P* value
RV dimensions			
RVAWD, cm	0.30 (0.30-0.31)	0.30 (0.30-0.30)	.319
RVDD, cm	1.75 (1.50-1.90)	1.40 (1.40-1.70)	.004*
RV systolic parameters			
TAPSE, mm	23.00 (20.00-25.00)	21.00 (20.00-24.00)	.311
S′, cm/s	13.00 (12.00-15.00)	13.00 (13.00-14.00)	.980
RV-GLS, %	−22.20 (−26.12 to −19.95)	−24.40 (−27.40 to −24.40)	.131
RV Diastolic parameters			
E′, cm/s	16.00 (14.00-17.00)	16.00 (17.00-19.00)	.044*
A′, cm/s	8.00 (7.75-11.00)	9.00 (9.00-12.00)	.272
E′/A′	1.60 (1.45-2.00)	1.90 (1.45-2.00)	.491
RV-MPI	0.30 (0.27-0.36)	0.30 (0.30-0.30)	.001*
RA strain			
GAS-positive, %	12.20 (9.38-16.62)	16.20 (11.50-19.00)	.095
GAS-negative, %	21.72 (18.10-29.55)	23.40 (15.79-29.40)	.935
Right heart Doppler			
PAP, mm Hg	31.50 (27.75-35.25)	30.00 (27.00-32.00)	.035*
PVTI, cm	19.55 (16.75-22.30)	21.00 (19.90-23.70)	.004*
PAT, ms	110.00 (92.00-123.25)	110.00 (104.00-122.00)	.370
PVR (TRV^2/VTI_{RVOT})	1.14 (1.00 -1.26)	0.86 (0.74- 1.00)	<.0001*
PEP, ms	52.00 (46.00-63.25)	41.50 (35.00-49.75)	<.001*
ET, ms	286.00 (276.00-300.00)	294.00 (266.00-317.00)	.361
PEP/ET	0.18 (0.16-0.22)	0.15 (0.11-0.20)	.005*

Abbreviations: ET, ejection time; GAS-negative, negative global atrial strain; GAS-positive, positive global atrial strain; MPI, myocardial performance index; PAP, pulmonary artery pressure; PAT, pulmonary acceleration time; PEP, pre-ejection period; RVOT, right ventricle outflow tract; PVR, pulmonary vascular resistance; PVTI, pulmonary velocity time integral; RA, right atrium; RVAWD, right ventricle anterior wall diameter; RVDD, right ventricle diastolic diameter; RV-GLS, right ventricle global longitudinal strain; RV, right ventricle; TRV, tricuspid regurgitation velocity; TAPSE, tricuspid annular plane systolic excursion.
*Statistically significant.

performance index was significantly higher in the patient group (*P* = .001, Table 2, Figure 3).

3.2.4 | RA strain

RA positive strain was lower in patients compared to control, but did not reach a statistically significant level (*P* = .09). The RA negative strain also did not show a significant difference between cases and control (Table 2).

3.2.5 | RV contractility, RV afterload, and RV stroke volume

The PEP and PEP/ET are mainly affected by the RV contractility and the RV afterload. In the studied cohort the estimated PAP, PEP, and PEP/ET ratio were significantly higher in patients when compared with controls (Table 2, Figure 4), while pulmonary velocity time integral (PVTI) was significantly lower in patients (*P* < .01, Table 2). TRV^2/VTI_{RVOT} was significantly higher in patients, when compared with the controls (*P* < .0001, Table 2). The peak expiratory flow (PEF) showed significant positive correlation with RV-E′ and PVTI (*r* = 0.287, *P* < .05, *r* = 0.288, *P* < .05, respectively), while PEF showed significant negative correlation with RVDD, RV-MPI, PVR, PEP, PEP/ET. Moreover, the TRV^2/VTI_{RVOT} showed significant positive correlation to PEP, PEP/ET, RV-MPI, RVDD. It also showed a significant negative correlation to PVTI (Table 4). This means that a higher PEF (with better pulmonary functions) will lower the PVR and RV afterload, which in turn will increase the RV stroke volume and improve RV diastolic function along with lessening or decreasing RV dilatation.

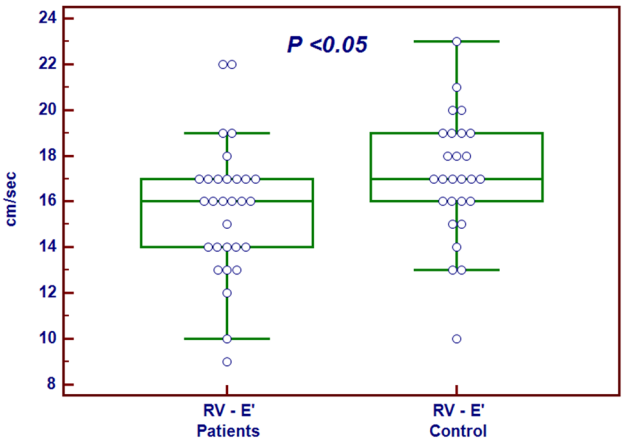

FIGURE 2 Box and whisker plots for RV-E′ velocity of patients and controls: RV-E′ velocity is significantly lower in patients denoting RV diastolic dysfunction (*P* < .05). RV, right ventricle [Color figure can be viewed at wileyonlinelibrary.com]

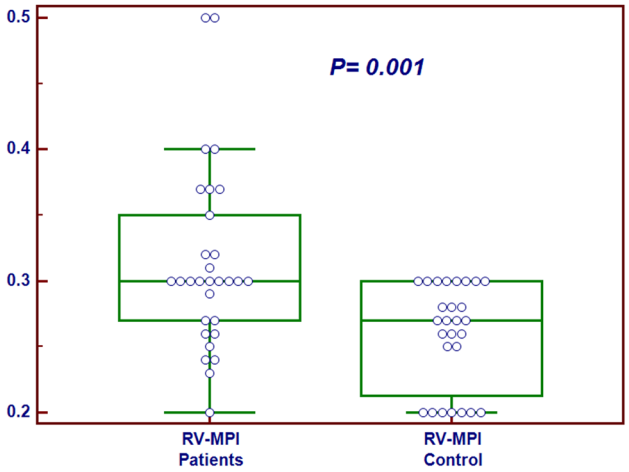

FIGURE 3 Box and whisker plots for RV-MPI of patients and controls: RV-MPI is significantly higher in patients ($P = .001$) compared with controls. MPI, myocardial performance index; RV, right ventricle [Color figure can be viewed at wileyonlinelibrary.com]

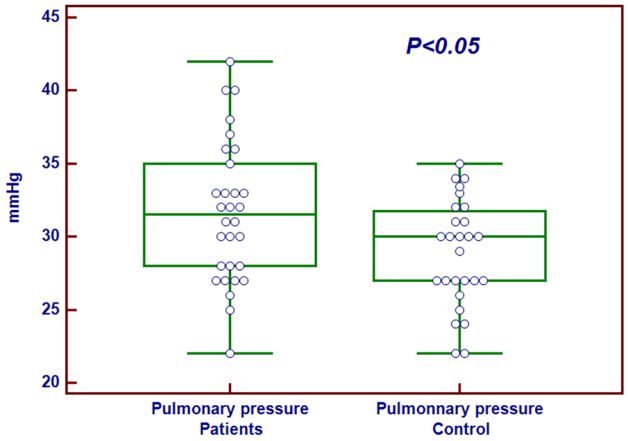

FIGURE 4 Box and whisker plots for pulmonary artery pressure (PAP) measured by echocardiography in patients and controls: The PAP is significantly higher in patients compared with controls ($P < .05$) [Color figure can be viewed at wileyonlinelibrary.com]

3.3 | LV parameters of the studied groups

3.3.1 | LV systolic function

The LV EF, FS, GLS, GRS, GCS, and S′ velocity did not differ significantly between the patient and control groups (Tables 3 and 4).

3.3.2 | LV diastolic function

The mitral E/A ratio, E′ septal velocity, E′ lateral wall velocity, and E/E′ did not show a significant difference between patients and controls (Table 3).

3.3.3 | Left ventricle-myocardial performance index

Although all the LV systolic and diastolic parameters did not show significant differences between patients and controls, the LV-MPI was significantly higher in patients ($P < .005$), when compared with the controls (Table 3).

4 | DISCUSSION

4.1 | Right heart parameters

Data regarding the right ventricular dimensions among asthmatic patients varies greatly in the literature.[23-28] In our cohort, patients had a greater degree of RV dilatation rather than of hypertrophy, when compared with the controls (Table 2), this may be due to the associated increase of PVR in these patients. Elevation of PVR which is frequently observed in patients with bronchial asthma may also lead to RV hypertrophy. In our cohort, RV hypertrophy was absent. This might be due to the fact that none of our patients had severe asthma. In addition, the relatively young age of our patients can explain the absence of right ventricular hypertrophy in our study.

The RV systolic function seems to be preserved in our cohort, since TAPSE obtained from conventional M-Mode, and S′ velocity obtained from TDI did not show significant differences between patients and controls. Data regarding the evaluation of the RV in asthmatic patients using deformation parameters such as RV strain is sparse.[29] In the present study, preservation of RV systolic function was confirmed by the use of the 2D STE derived RV strain which did not differ significantly between patients and controls. Preservation of RV systolic function was among the parameters reported by previous studies in asthmatic patients.[23-26] In contrast to our study, Shedeed reported RV systolic dysfunction in asthmatic patients.[28] The discrepancy in the results regarding RV function may be again attributed to differences in the severity and duration of asthma among the studied populations.

4.1.1 | RV diastolic function

In the examined cohort, the diastolic RV dysfunction was noticed since the tricuspid annulus (E′) derived from TDI was significantly lower in asthmatic patients, when compared with the controls. Several studies reported RV diastolic dysfunction in asthmatic patients[6,24-28] even before any impairment of RV systolic function.

4.1.2 | Right ventricle-myocardial performance index

In this study, the RV-MPI of the asthmatic patients was significantly higher compared with the control group. The significantly higher MPI among asthmatic patients may be attributed to diastolic dysfunction. In favor of this assumption speaks the preserved RV systolic and early diastolic dysfunction discussed earlier among the studied cohort. Several studies reported elevated RV-MPI in asthmatic patients.[6,24-26,28,30]

TABLE 3 LV parameters of studied groups

Parameters	Patients (n = 30)	Control (n = 27)	*P* value
M-mode			
FS, %	37.00 (33.70-42.00)	36.00 (35.00-39.00)	.911
EF, %	67.00 (63.00-73.00)	66.00 (65.00-70.00)	.943
Systolic parameters—TDI			
S′—septum, cm/s	7.50 (7.00-8.25)	13.00 (13.00-15.00)	.115
S′—lateral wall, cm/s	9.00 (8.00-10.00)	9.00 (8.00-10.00)	.510
Diastolic parameters			
Mitral E, cm/s	89.50 (85.25-99.25)	90.00 (83.00-106.00)	.810
Mitral A, cm/s	52.00 (44.70-60.00)	47.00 (40.00-55.00)	.280
Mitral E/A	1.74 (1.59-1.95)	1.86 (1.60-2.26)	.198
E′—septum, cm/s	13.00 (12.00-14.00)	13.00 (13.00-15.00)	.422
E′—lateral wall, cm/s	17.00 (15.70-20.00)	18.00 (15.00-19.00)	.936
A′ septum, cm/s	6.00 (5.70-7.00)	6.00 (5.00-7.00)	.787
A′ lateral wall, cm/s	6.00 (5.00-8.00)	6.00 (5.00-8.00)	.890
E/E′	6.99 (6.26-7.84)	6.76 (6.07-7.92)	.743
MPI	0.39 (0.30-0.45)	0.30 (0.30-0.37)	.003*
2D-STE			
GLS	−21.35 (−22.38 to −19.45)	−21.70 (−23.70 to −19.70)	.379
GCS	−18.40 (−20.60 to −16.10)	−17.80 (−21-0.00 to −16.30)	.660
GRS	−24.15 (−29.22to −18.58)	−21.30 (−23.90 to −18.20)	.087

Abbreviations: 2D-STE, 2-dimensional speckle tracking echocardiography; EF, ejection fraction; FS, fractional shortening; GCS, global circumferential strain; GLS, global longitudinal strain; GRS, global radial strain; LV, left ventricle; MPI, myocardial performance index; TDI, tissue Doppler imaging.
*Statistically significant.

4.1.3 | RA strain

To our knowledge, the present study is the first one that evaluates the RA function among children with bronchial asthma. Although the RA positive strain, which reflects atrial reservoir function was lower in patients compared with controls, this difference did not reach a statistically significant level ($P = .09$). This might reflect very early subtle decline in systolic RV function, since the atrial reservoir function is mainly affected influenced by two factors, namely ventricular systolic function and atrial relaxation property.[31]

RA negative strain reflecting RA pump function did not significantly differs in patients when compared with controls. The RA negative strain is mainly affected by the RV end-diastolic pressure. Since most of our patients had mild asthma, the RV end-diastolic pressure in these patients may be not elevated enough to the degree that could affect the RA negative strain. Further studies are needed on larger groups with different severities to know the real effects of different severities of bronchial asthma on the RA strain.

TABLE 4 Correlation between right heart parameters and PEF

Correlated parameters	Correlation coefficient (*r*)	*P* value
PEF		
RVDD	−0.367	.005*
RV-E′	0.287	<.050*
RV-MPI	−0.285	<.0 50*
PVR (TRV^2/VTI_{RVOT})	−0.481	<.0001*
PVTI	0.288	<.050*
PEP/ET	−0.456	<.0001*
PEP	−0.414	.001*
PVR (TRV^2/VTI_{RVOT})		
PVTI	−0.366	<.01*
PEP	0.438	.001*
PEP/ET	0.5421	.001*
RV-MPI	0.310	.019*
RVEDD	0.445	.001*

Abbreviations: ET, ejection time; MPI, myocardial performance index; PAP, pulmonary artery pressure; PEF, peak expiratory flow; PEP, pre-ejection period; PVR, pulmonary vascular resistance; PVTI, pulmonary velocity time integral; RV, right ventricle; RVDD, right ventricle diastolic diameter; TRV, tricuspid regurgitation velocity.
*Statistically significant.

4.1.4 | Pulmonary artery pressure and PVR

As mentioned before bronchial asthma can increase the pulmonary vascular resistance and pulmonary artery pressure by several mechanisms. In our study, PVR and PAP were higher in the patients' group (compared with the control group). Several studies reported similar results to ours.[7,24] Additionally, pulmonary VTI was significantly lower in our patients when compared with controls. This might reflect an increase in the RV afterload secondary to a higher pulmonary vascular resistance. Özkan et al[29] reported similar findings. Another possible explanation for the decreased VTI among our patients when compared with controls is the relatively higher heart rate frequently observed in asthmatic patients with the use of bronchodilators; however, the median heart rate in patients group was just 6 beats per minute (BPM) higher than control and did not achieve statistical significance. Hedlin et al[32] reported decreased stroke volume in asthmatic children with the provocation of asthma that increased after inhaled salbutamol.

4.1.5 | RV afterload

The PEP and PEP/ET are parameters reflecting mainly the RV contractility and the RV afterload. In the present study, both were significantly higher in patients when compared with the controls. We assume that RV contractile dysfunction is not the culprit for such finding since our patients were young and had only mild to moderate asthma. The elevated PEP and PEP/ET observed in the studied cohort could be in deed related to a possible increased RV afterload. In addition, the TRV^2/VTI_{RVOT} showed significant positive correlation with PEP and PEP/ET. This might be explained by the possible increased PVR associated with bronchial asthma. Hirschfeld et al[33] reported significant correlation between RV PEP/ET and PVR in pediatric patients who underwent cardiac catheterization ($r = 0.69$),while Özkan et al[29] did not report a significant difference between their patients and controls in relation to RV PEP/ET ratio. The significant correlation between the peak expiratory flow (PEF) and other right heart parameters may reflect the relationship between the pulmonary function, the PVR and the right heart functions.

4.2 | Left ventricular function

4.2.1 | LV systolic function

In our study, the LV systolic function was preserved in the patient group. Ozdemir et al[30] reported similar findings regarding EF and S′ velocity at the mitral annulus, wh ile Tuleta et al[34] reported diminished LV longitudinal strain in patients with severe and mild to moderate asthma. This is in contrast to our patients who mostly had mild asthma.

4.2.2 | LV diastolic function

There was no significant difference regarding mitral E/A ratio, E′ septal velocity, E′ lateral wall velocity and E/E′ between the patient and control groups denoting preserved LV diastolic function in asthmatic patients. Elmasry et al reported LV diastolic dysfunction in the form of decreased mitral E/A ratio during acute exacerbation of asthma that returned to normal after the resolution of an acute asthmatic attack. This is consistent with our findings as echocardiography was done between episodic attacks and not during the acute attacks.[35] Hirono et al reported LV diastolic dysfunction in asthmatic patients receiving long-acting oral β_2 agonists.[36] Our cohort, in contrast, did not receive long acting oral β_2 agonists, and were only treated with PRN salbutamol inhalant and inhaled corticosterods (Table 1). Despite conventional echocardiography, TDI and 2D-STE did not show significant systolic or diastolic dysfunction in asthmatic children when compared to controls; the LV-MPI was significantly higher in the patient group. This might reflect very early subtle subclinical left ventricular dysfunction, secondary to the observed right ventricular diastolic dysfunction. These subtle changes might be mediated by the ventricular interdependency action of the interventricular septum.

4.3 | Study limitations

The main limitation of this study was the relatively small number of patients. In addition, the study did not include different severities of asthma. Moreover, the assumption of increased pulmonary vascular resistance was not proven by invasive hemodynamic studies. The gold standard for evaluation of the PVR is cardiac catheterization. Such a procedure is not indicated among patients with mild to moderate bronchial asthma. In this study, PVR was evaluated using the formula: $PVR = TRV^2/VTI_{RVOT}$. By using this formula, the reported elevation of PVR may be related to the decreased PVTI associated with relatively higher heart rates and not only the impact of the disease on the pulmonary vasculature.

5 | CONCLUSION

Pediatric patients with mild to moderate bronchial asthma may have early RV diastolic dysfunction that could be secondary to increased PVR and increased RV afterload. The RV, RA and LV strain of these patients seems to be preserved among this cohort.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ORCID

Gaser Abdelmohsen http://orcid.org/0000-0002-0361-2921

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