RESEARCH ARTICLE

Can speckle tracking of right ventricle add value for evaluation of asthma severity in children?

Ahmed Mohammad Abbas[1], Hany Hussein Mousa[2], Reda Biomy[3], Osama Elagamy[4]

Abstract

Objective: To investigate myocardial deformation by tracking speckles along with evaluation of cardiac function using conventional and tissue Doppler imaging.

Method: The case-control study was conducted at Kafrelsheikh University Hospital, Egypt, from September 2019 to May 2022, and comprised asthmatic children and healthy controls matched for age and gender. After taking family history of asthma, assessments were made for bronchial asthma treatment and severity. Clinical examination and pulmonary function tests were performed along with tissue Doppler imaging and speckle tracking. Global left ventricular and right ventricular strains were measured. Data was analysed using SPSS 22.

Results: Of the 120 subjects, 60(50%) were cases; 33(55%) males and 27(45%) females with mean age 9.4±2.91 years. The remaining 60(50%) were controls; 34(56.7%) males and 26(43.3%) females with mean age 9.7±2.99 years (p>0.05). Among the cases, 36(60%) had moderate severity and 24(40%) had mild asthma. Family history was positive in 11(18.3%) cases and negative in 49(81.7%). There was no significant difference in terms of conventional echocardiography between the groups (p>0.05). There was impairment in right ventricular diastolic function in the cases, with lateral tricuspid E` velocity significantly lower (p<0.05) and isovolumetric relaxation time significantly higher than the controls (p=0.001). There was impairment of systolic function of the right ventricle in the cases compared to the controls (p=0.001). Right ventricular peak longitudinal systolic stress cut-off value distinguishing the controls from the cases was -20.4 with sensitivity 85% and specificity 63%. The cut-off value distinguishing mild from moderate asthmatic cases was -19.8 with sensitivity 83% and specificity 91%.

Conclusion: Speckle tracking echocardiography could detect very early subtle right ventricular systolic dysfunction. Right ventricle dysfunction worsened with the severity of asthma.

Keywords: Hypertension, Pulmonary, Echocardiography, Respiratory, Asthma, Hypoxia.

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Introduction

Bronchial asthma is a common chronic immunological disease affecting children.[1] It causes recurrent attacks of hypoxaemia with the release of inflammatory mediators that may lead to pulmonary vasoconstriction and elevated pulmonary vascular resistance[2] that may be followed by right ventricular (RV) dysfunction and pulmonary hypertension (PHT).[3] The assessment of RV function is difficult by conventional methods due to its position posterior to the sternum, leading to inadequate image quality, especially in patients with hyperinflated lung disease. Besides, accurately locating the boundary of the anterior wall's endocardium is considered a problem as the trabeculations are coarser compared to the left ventricle (LV).[4] Quantitative measurements of regional myocardial velocities are more sensitive in the assessment of RV function using tissue Doppler study, but it is affected by translational cardiac movement and s angle-dependent.[5] Two-dimensional (2D) speckle tracking overcomes tissue Doppler limitations and is considered superior in detecting cardiac dysfunction.[6]

The current study was planned to assess the cardiac function in children with bronchial asthma using speckle tracking echocardiography.

Subjects and Methods

The case-control study was conducted at Kafrelsheikh University Hospital, Egypt, from September 2019 to May 2022. After approval from the institutional ethics review committee, the sample was raised using random sampling technique from among asthmatic children aged 4-14 years coming for follow-up at the paediatric outpatient clinic. Asthmatic children were not enrolled during exacerbations to exclude changes in ventricular function secondary to transient increase in pulmonary artery pressure and to avoid hyperinflated lung which could lead to a poor window for echocardiography. Also excluded were children outside the age bracket, those with known cardiac disease, marked congenital anomalies, collagen disease or any major illness affecting the cardiac function, obese with body mass index (BMI) > 95% for age and gender, and

[1,4] Department of Paediatrics, Kafrelsheikh University, Egypt.

[2] Department of Chest, Kafrelsheikh University, Egypt.

[3] Department of Cardiology, Kafrelsheikh University, Egypt.

Corrospondience: Ahmed Mohammad Abbas

email: Ahmed_Abbas@med.kfs.edu.eg

children with severe persistent asthma. A group of healthy children matched for age and gender were enrolled as control. After taking written informed consent from the parents of all the children, both groups were subjected to detailed history, including duration of asthma and family history, and complete clinical examination.

Pulmonary function test was performed, including forced vital capacity (FVC), forced expiratory volume in the first second of FVC (FEV1) and the Tiffeneau-Pinelli index (FEV1/FVC).[7] Measured values were percentage of the predicted values. The cases were subjected to bronchodilator reversibility test 15-20 minutes after inhalation of 400µg salbutamol (Geratherm Spirostik). Assessment and classification of asthma severity were done according to the national asthma education and prevention programme (NAEPP).[8]

Intermittent asthma was defined as symptoms <2 times per week and asymptomatic in between the attacks. Nocturnal symptoms <2 a month. FEV1 ³80% predicted.

Mild persistent asthma was defined as symptoms of wheezing, cough or difficult breathing 3-6 times a week. Activity level may be affected. Nocturnal symptoms >2 per month. FEV1 ³80% predicted.

Moderate persistent asthma was characterised by daily symptoms affecting activity during flare-ups. Nocturnal symptoms ³5 times a month. FEV1 60-80% predicted.

Sever persistent asthma was defined as continuous symptoms limiting physical activity with frequent nocturnal symptoms. FEV1 60% or less of normal values.

Echocardiography (Philips Affiniti 50C) was done with simultaneous electrocardiogram (ECG) recording and probe 3 or 5MHz. Parameters noted were left ventricular posterior wall thickness (LVPW), interventricular septum (IVS), left ventricular internal diameter during diastole (LVIDd) and during systole (LVIDs). Fractional shortening (FS) and ejection fraction (EF) were measured from the parasternal short axis M-Mode. Tricuspid annular plane systolic excursion (TAPSE) was measured at apical 4-chamber view using 2D M-Mode, positioning the cursor on the lateral tricuspid annulus near the free RV wall. Tricuspid peak early (E) and peak late (A) velocities were measured by examining the tricuspid valve using pulsed wave Doppler in the apical 4-chamber view. Estimated systolic pulmonary artery pressure (ESPAP) was obtained by continuous wave Doppler, measuring maximum regurgitation velocity at the tricuspid valve, then assumed right atrial pressure of 10mmHg was added to its value. Pulsed wave tissue Doppler echocardiography was performed in apical 4-chamber view with frame rate >150 frames per second, using pulsed wave with curser positioned in the lateral and medial borders of tricuspid annulus. Systolic S` and diastolic E` and A` wave velocities were measured at the RV free wall. Isovolumetric relaxation time (IVRT), isovolumetric contraction time (IVCT) and ejection time (ET) were also measured. Myocardial performance index (MPI) was calculated, using the equation: (IVRT+IVCT) / ET.[9]

All children were subjected to 2D speckle tracking. The gain setting was optimised, grey scale frame rate was kept between 30 and 70 frames per second. With ECG gating, 3 cardiac cycles were acquired for each loop. LV global longitudinal strain (GLS) was obtained from apical long axis, apical 2-chamber and apical 4-chamber views. RV GLS was acquired from the apical 4-chamber view. Endocardial border was traced in its entirety, starting from one end of the valve annulus to the other end. Regions of interest (ROI) were generated by Q Lab version 10 software using Automated cardiac motion quantification (aCMQ) option for calculation of longitudinal strain parameters, while the entire myocardial thickness and width were manually adjusted (Figures 1-2).

Data was analysed using SPSS 22. For normally distributed variables, independent samples t-test was used to compare the difference between two independent groups, while one-way analysis of variance (ANOVA) was used to compare three or more independent groups. For non-parametric dependent variables, Mann-Whitney U test was used to compare two independent groups. For qualitative variables, chi-square and Fisher tests were used. Receiver operating characteristic (ROC) analysis included ROC curve, area under the curve (AUC), significance and the best cut-off value. In addition, sensitivity and specificity were calculated at the optimal cut-off value. $P<0.05$ was considered statistically significant.

Results

Of the 120 subjects, 60(50%) were cases; 33(55%) males and 27(45%) females with mean age 9.4±2.91 years. The remaining 60(50%) were controls; 34(56.7%) males and 26(43.3%) females with mean age 9.7±2.99 years ($p>0.05$). Among the cases, 36(60%) had moderate severity and 24(40%) had mild asthma. Family history was positive in 11(18.3%) cases and negative in 49(81.7%). Spirometry measurements were significantly lower in asthmatic children (Table 1).

LV parameters showed no significant difference between the groups ($p>0.05$). LV GLS showed no significant difference either ($p>0.05$).

Estimated pulmonary artery pressure was higher among

Table-1: Demographic data.

Parameters	Cases (n=60)	Control (n=60)	*p-value*
Age	9.4 ± 2.91	9.7 ± 2.99	0.504
Females, n (%)	27 (45%)	26 (43.3%)	0.854
Height, cm	126 ±15.8	133 ± 16.8	0.014*
Weight, kg	27.5 ± 9.9	34 ± 11.2	0.001*
Heart rate	82 ± 7	82.8 ± 6.9	0.85
Respiratory rate	25.9± 3.8	26.2 ± 4.2	0.74
Spirometry			
FVC ±	94 (84-102)	92.5 (79-98)	0.1
FEV1±	82 (70-94)	89 (80-96)	<0.001*
FEV1/FVC	0.88 (0.7-1)	0.96 (0.85-1)	<0.001*
Severity, n (%)			
Mild	24 (40)		
Moderate	36 (60)		
Asthma treatment,	n (%)		
Step 1	30 (50)		
Step 2	24 (40)		
Step 3	5 (10)		
Family history,	n (%)		
Positive	11 (18.3)		
Negative	49 (81.7)		

* Statistically significant. ± percentage predicted to normal values.
FVC: Forced vital capacity, FEV1: Forced expiratory volume in the first second.

Table-2: Inter-group comparison regarding biventricular function.

Parameters	Cases (n=60)	Control (n=60)	*p-value*
Left ventricle			
Ejection fraction %	67 (61-72)	67 (63-74)	0.619
Fractional shortening %	38 (31-42)	38 (35-45)	0.55
LV-GLS	-20.8 (0.8)	- 20.76 (0.86)	0.381
EPAP, mmHg	21 (17-26)	20 (15-25)	0.057
Main PAD, cm	1.97 (1.34-2.6)	1.91 (1.34-2.5)	0.209
RV dimensions			
RV wall thickness, cm	0.34 (0.045)	0.32 (0.04)	0.058
RVDD, cm	2.75 (1-3.5)	2.4 (0.9-3.5)	0.046*
RV systolic function			
TAPSE, cm	2 (1.8-2.5)	2 (1.7-2.4)	0.112
Lateral tricuspid S` peak velocity, cm/sec	11.7 (1.34)	12 (1.23)	0.374
PLSS %	-19.5 (-16.5- 32.2)	- 21.2 (-18.4-25)	0.001*
RV diastolic function			
Lateral tricuspid E` peak velocity, cm/sec	13.9 (1.6)	15.1 (2.19)	0.001*
Lateral tricuspid A` peak velocity, cm/sec	10.35 (8-14.5)	11 (8-14.4)	0.018*
IVRT, m.sec	48 (36-66)	39 (36-55)	0.001*
MPI %	0.42 (0.34-0.49)	0.4 (0.30-0.47)	0.005*

LV-GLS: Left ventricular global longitudinal strain, ESPAP: Estimated systolic pulmonary artery pressure, PAD: Pulmonary artery diameter, RV: Right ventricle, RVDD: Right ventricle diastolic diameter, TAPSE: Tricuspid annular plane systolic excursion, PLSS: Peak longitudinal systolic strain, IVRT: Isovolumetric relaxation time, MPI: Myocardial performance index.

Table-3: Receiver operating characteristic (ROC) curve of echocardiographic findings of interest.

ROC analysis showing the cut-off values of RV studies distinguishing healthy from asthmatic children.

Parameters	Cut-off value	specificity	sensitivity	AUC	*p-value*
IVRT	237 m.sec	0.76	0.71	0.78	<0.001*
MPI	0.39	0.65	0.61	0.65	0.004*
RV-PLSS	-20.4	0.63	0.85	0.68	0.001*

ROC analysis showing the cut-off values of RV studies distinguishing mild from moderate asthmatic children.

Parameters	Cut-off value	specificity	sensitivity	AUC	*p-value*
IVRT	220 m.sec	0.41	0.75	0.56	0.398
MPI	0.405	0.65	0.61	0.54	0.316
RV-PLSS	-19.8	0.91	0.83	0.95	0.001*

AUC: Area under the curve, IVRT: Isovolumetric relaxation time, MPI: Myocardial performance index, RV: Right ventricle, PLSS: Peak longitudinal systolic strain.

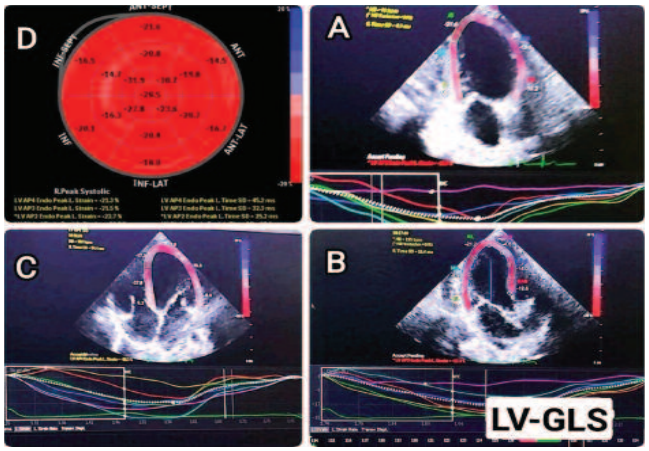

Figure 1: (A) Apical 2-chamber view. (B) Apical long axis view of left ventricle (LV) global longitudinal strain (GLS). (C) apical 4-chamber view. (D) Bull's eye of GLS.

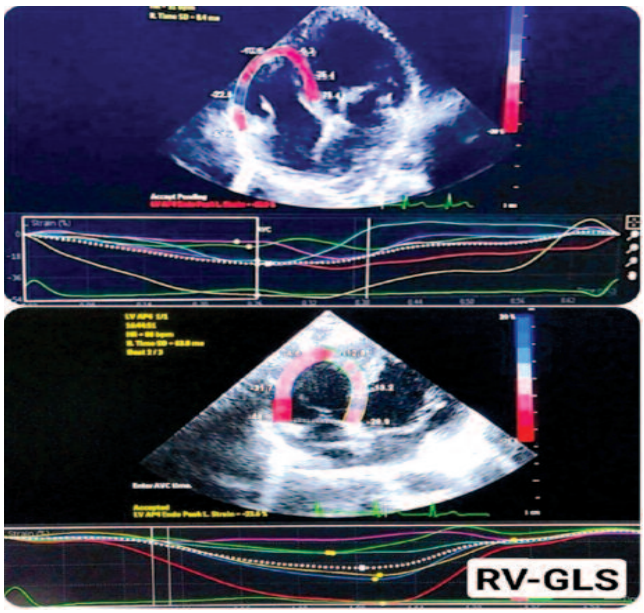

Figure 2: Speckle tracking of right ventricular (RV) global longitudinal strain (GLS).

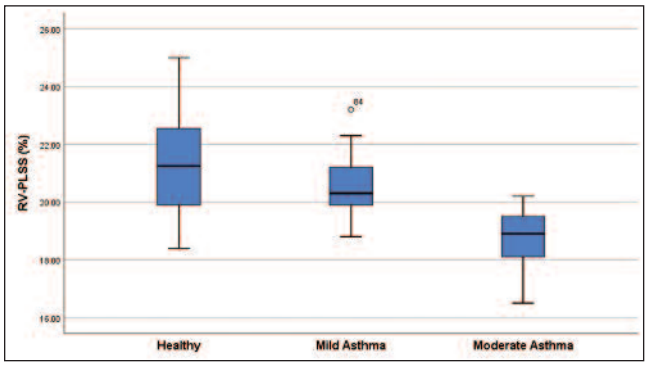

Figure 3: Box-plot showing distribution of right ventricular (RV) global longitudinal strain (GLS) among the subgroups.

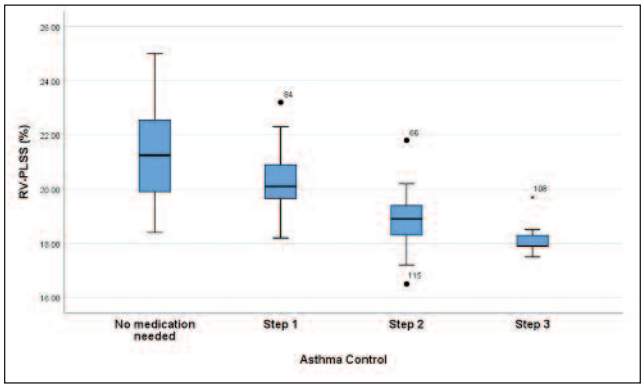

Figure 4: Box-plot showing distribution of right ventricular (RV) global longitudinal strain (GLS) among the subgroups.

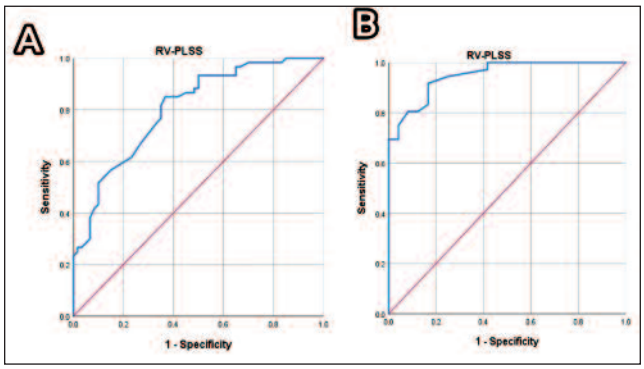

Figure 5: Receiver operating characteristics (ROC) curve analysis showing the right ventricle (RV) PLSS cut-off values (A) Distinguishing healthy from asthmatic children. (B) Detecting moderate asthma in asthmatic group.

the cases, but the difference was non-significant (p=0.057). RV end diastolic diameter was significantly higher among the cases (p<0.05), while wall thickness was not significantly different (p>0.05). RV diastolic function was affected in the cases as they showed significantly lower tricuspid early and late diastolic velocities (E`, A`) (p=0.004, p=0.018) and prolonged IVRT (p=0.001). Although both conventional echocardiography and tissue Doppler showed that RV systolic function was not affected with tricuspid S` velocity and TAPSE now show significant difference between the groups (p>0.05), speckle tracking of RV showed significant lower peak longitudinal systolic stress (PLSS) among the cases (p=0.001) (Table 2).

RV PLSS was significantly impaired by the severity of asthma (p<0.001). There was moderate association between RV GLS and asthma severity subgroups (Eta=0.642), with large effect size (0.412) showing that about 41.2% of variance of RV GLS can account for asthma severity (Figures 3-4).

ROC curve showed the cut-off point differentiating between healthy and asthmatic children was -20.4 with specificity 63% and sensitivity 85% (p=0.001). The cut-off point differentiating mild from moderate asthma was -19.8 with specificity 91% and sensitivity 83% (p=0.001), while AUC 0.95 indicated good quality of the test (Table 3, Figure 5).

Discussion

Asthma is a common chronic immunological disease affecting children.[1] It is characterised by hyper-reactivity of the airways resulting in symptoms, including difficult breathing, cough and wheezy chest and a high burden on the affected families.[8]

In the current study, LV function was preserved in the asthmatic group by conventional and speckle tracking imaging. Abdelmohsen et al.[6] reported similar results, while Tuleta et al.[11] reported diminished LV GLS in moderate to severe asthma.

Asthmatic children in the current study showed RV dilatation with the absence of ventricular wall hypertrophy in comparison with the healthy group. Although estimated pulmonary artery pressure was not elevated in the asthmatic group, it did not exclude past episodes of exacerbation with attacks of hypoxaemia and transient increase of pulmonary artery pressure which may affect RV. RV wall hypertrophy was not frequently seen among the cases in the current study, which was perhaps due to the young age group and the exclusion of severe asthma patients.

RV diastolic function was affected in the asthmatic group. Tricuspid annulus early and late diastolic velocities E`, A` were significantly lower in the cases than the controls. IVRT was higher in asthmatics. Many studies have reported the same results. RV MPI, which has gained acceptance in evaluating both systolic and diastolic ventricular functions, was significantly higher in asthmatics. Multiple studies have reported elevation in RV MPI in asthma.[6, 11, 12]

RV systolic function seemed to be preserved by both conventional and tissue Doppler imaging. TAPSE and tricuspid S` velocity showed no significant difference between asthmatic and healthy children. This was not the same with 2D speckle tracking of RV GLS which showed

significant difference between the groups, indicating subtle systolic dysfunction. Systolic dysfunction of RV in asthmatic children has previously been reported.[13] Another study reported that RV GLS did not show significant difference between the patients and the controls, which is in contrast to the current findings. The study found that right atrial positive strain was lower in asthma, but not significantly. Because the atrial reservoir function was influenced by atrial relaxation property and ventricular systolic function, very early subtle decrease of RV systolic function was suspected.[6] The difference in the results with the current study is perhaps due to differences in duration and severity of asthma in the studied populations.

In the current study, there was significant decrease in RV systolic function which increased with the severity of asthma. The current study found cut-off points to differentiate between the cases and the controls as well as between mild and moderate asthma, and AUC suggested it was a good test. Progress in treatment of asthma is relatively slow and guidelines have mostly recommended empirical approaches.[1] Certain complications such as cardiac affection can be added for stepping up in asthma treatment, especially if detected early before the appearance of clinical manifestations or changes in conventional echocardiographic parameters. Speckle tracking seems to have promise in detecting early subtle RV systolic dysfunction.

Limitations

The current study has limitations, like sample size was not calculated, which could influence the power of the study. Besides, a small sample size is also not representative of the overall asthmatic population. Also, using speckle tracking technique has its challenges due to lack of standardization of parameters to be measured and of specific software packages in use to obtain such measures.[15] Finally, all speckle tracking measurements require high capability in terms of image acquisition, obtaining correct endocardial border delineation, obtaining suitable echocardiographic views, inter-observer and intra-observer variability. As such, the findings depend critically on the machine with which the analyses are performed.

Conclusion

Early impairment of cardiac function in children with asthma could be detected by tissue Doppler and speckle tracking imaging at a stage when conventional echocardiography may still be presenting normal parameters. Speckle tracking echocardiography could detect very early subtle RV systolic dysfunction. RV dysfunction increased with the severity of asthma.

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