RESEARCH ARTICLE

Tissue doppler echocardiography as a predictor of early subclinical right ventricular diastolic dysfunction in asthmatic children.

Ahmed Mohammad Abbas[1], Hany Hussein Mousa[2], Reda biomy[3], Mohamed AbdelGhafar Hussein[4], Heba Mohammad Reyad[5], Osama Elagamy[6]

Abstract

Objective: To assess the effect of asthma in children on systolic and diastolic functions of the heart, and to explore the relationship between the two.

Methods: The case-control study was conducted at Kafrelsheikh University Hospital, Egypt, from September 2019 to May 2022, and comprised asthmatic children of either gender aged 5-15 years and healthy controls matched for age and gender. The participants were subjected to detailed history, complete examination, spirometry evaluation and conventional and tissue Doppler echocardiography. Myocardial performance index was calculated and compared. Data was analysed using SPSS 22.

Results: Of the 120 subjects, 60(50%) were cases; 33(55%) boys and 27(45%) girls with mean age 9.4±2.9 years (range: 5-15 years). The remaining 60(50%) subjects were controls; 34(56.6%) boys and 26(43.3%) girls with mean age 9.7±2.9 years (range: 5-15 years). Left ventricular dimensions, estimated pulmonary artery pressure, and right ventricular dimensions showed no significant inter-group differences (*p*>0.05), but right ventricular end diastolic diameter was significantly higher in the cases than the controls (*p*=0.046). Tissue Doppler showed that lateral annular peak Ȇ, Â, isovolumetric relaxation time and myocardial performance index values were significantly different between the groups (*p*<0.05).

Conclusion: Tissue Doppler echocardiography could detect subtle right ventricular diastolic dysfunction in asthmatic children even with no clinical symptoms and normal findings on conventional echocardiography.

Keywords: Pulmonary artery, Echocardiography, Doppler, Asthma, Spirometry. **DOI: 10.47391/JPMA.EGY-S4-31**

Introduction

Asthma is a chronic inflammatory disorder of the airways characterised by their hyper-reactivity to various stimuli, like irritants and allergens, that results in different symptoms, including cough, wheezy chest and difficult breathing. Asthmatic children are subjected to repeated attacks of hypoxaemia with chronic inflammation, including release of various cytokines and mediators, which may lead to narrowing of pulmonary vasculature. Right ventricular (RV) enlargement and hypertrophy may occur with RV impairment. Little is known about affection of RV function in the early course of asthma, and it is difficult to assess RV function using conventional echocardiography imaging technique. Difficulties are present in the estimation of RV function since its position posterior to the sternum lead to inadequate image quality, especially in patients with chronic lung disease and those having frequently hyper-inflated lungs. 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). Tissue Doppler echocardiography (TDE) measures the regional myocardial velocities and intervals of diastole and systole. It can accurately detect subclinical RV abnormalities missed by standard echocardiography in asthmatic children. Asthma is considered one of the most common childhood chronic diseases, impairing the patient's quality of life (QOL), irritating the families, and incurring high costs to society and the healthcare system**.** In the Middle East, the prevalence of bronchial asthma ranges 5-23% and has been previously reported to be lower than in the developed countries. This increases the need for accurate non-invasive tests to detect early secondary cardiac affection for proper management and to improve QOL. The current study was planned to assess the effect of bronchial asthma on cardiac function using TD imaging.

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 from among asthmatic children of either gender aged 5-15 years who were

[1,4-6] 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

selected randomly during their follow-up at the paediatric outpatient clinic. Healthy controls matched for age and gender were also enrolled. Informed consent was obtained from all the participants.

Those outside the age range, with known cardiac disease, severe infection or exacerbation or having received theophylline within the preceding month, known hypertensives, obese with body mass index (BMI) >95% for age and gender, major congenital anomalies, thoracic deformities or neuromuscular disorders, and subjects refusing to participate were excluded.

The enrolled children were subjected to detailed history, including consanguinity, general and local chest examination, spirometry using Spirostik Complete (Geratherm Respiratory AG, Germany) for forced expiratory volume 1 (FEV1) / forced vital capacity (FVC), and oxygen saturation measurement by pulse oximetry.

Intermittent asthma was defined as symptoms <2 times per week and the patient being asymptomatic between the attacks; nocturnal symptoms <2 a month; and FEV1 ^{3}80% predicted.

Mild persistent asthma was defined as symptoms of wheezing, cough or difficult breathing 3-6 times a week with affection of activity level; nocturnal symptoms >2 per month; and FEV1 ^{3}80% predicted.

Moderate persistent asthma was characterised by daily symptoms affecting activity during flare-ups; nocturnal symptoms ^{3}5 times a month; and FEV1 60-80% predicted.

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

Echocardiographic evaluation was done using a 50C machine (Philips Affiniti) with simultaneous electrocardiogram (ECG) recording at the institutional paediatric echocardiography laboratory. Conventional echocardiographic measurements were obtained, and aortic and left atrial (LA) dimensions were measured, like LV posterior wall (LVPW) thickness, interventricular septum (IVS), LV internal diameter during diastole (LVIDd) and during systole (LVIDs). Also, fractional shortening (FS) and ejection fraction (EF) were measured from the parasternal short axis M-Mode. RV-filling indices from apical 4-chamber view were noted using pulsed wave Doppler placed at tricuspid valve opening with obtaining tricuspid peak early velocity E and peak late velocity A. tricuspid annular plane systolic excursion (TAPSE) was measured from the apical 4-chamber view in 2-dimensional (2D) M-Mode, placing the cursor on the tricuspid lateral annulus close to the free RV wall. Estimated systolic pulmonary artery pressure was calculated using maximum regurgitation velocity at the tricuspid valve by continuous Doppler, and adding an assumed right atrial (RA) pressure of 10mmHg to its value.

TD study recorded motions of the tricuspid annulus at a frame rate of 90-150 frames per second using pulsed wave in the apical 4-chamber view with curser positioned in the lateral border of tricuspid annulus, measuring two negative velocities occur during the movement of annulus towards the cardiac base during diastole; Ê` (early phase) and Â` (late phase of diastole). During systole, with the movement of annulus towards the apex, a major systolic positive velocity S` was recorded (Figure 1). Velocities were assessed at the RV free wall, and isovolumetric relaxation time (IVRT), isovolumetric contraction time (IVCT) and ejection time (ET) were measured. Myocardial performance index (MPI) was calculated, equal to (IVRT+IVCT) / ET.

Data was analysed using SPSS 22. For normally distributed variables, independent samples t-test was used to compare the difference between two independent variables, while one-way analysis of variance (ANOVA) was used to compare three or more independent variables. In non-parametric dependent variables, Mann-Whitney U test was used to compare two independent groups. Chi-square test and Fisher test were used to calculate the difference between qualitative variables.

P<≤0.05 was considered statistically significant, and *p*<0.001 was considered highly significant.

Results

Of the 120 subjects, 60(50%) were cases; 33(55%) boys and 27(45%) girls with mean age 9.4±2.9 years (range: 5-15 years). The remaining 60(50%) subjects were controls; 34(56.6%) boys and 26(43.3%) girls with mean age 9.7±2.9 years (range: 5-15 years). The cases were significantly shorter in height and lower in weight compared to the controls (*p*<0.05), but vital signs, including respiratory rate (RR), heart rate (HR) and blood pressure (BP), did not differ significantly (*p*>0.05).

LV parameters had no significant difference between the groups, and the same was the case with LA diameter, , EF and fractional shortening (Table 1).

RV end diastolic diameter (RVEED) was significantly higher in the cases than the controls (*p*=0.046). (Table 2).

TDE showed that lateral annular peak E`, A`, IVRT and MPI values were significantly different between the groups (*p*<0.05) (Table 3).

Table-1: Comparison between patients and controls regarding clinical data.

Parameter	Patients (n=60)	Control (n=60)	test	*p-value*
Gender n(%)				
Male	33(55)	34(56.6)	X2	
Female	27(45)	26(43.3)	0.034	0.854
Age	9.4 (5-15)	10 (5-15)	MW	0.5
Weight	27 (16-55)	33 (18-58)	MW	0.001
Height	126 (97-156)	135 (100-163)	MW	0.014
BMI	16.8±2.46	18.5±2.1	t	<0.001
Vitals				
RR	24 (20-34)	25 (18-35)	MW	0.746
HR	82 (68-95)	81 (69-95)	MW	0.854
Systolic BP	110 (100-115)	110 (100-115)	MW	0.526
Diastolic BP	71 (60-75)	73 (60-75)	MW	0.946
LAD (mm)	28.2 (16-55)	33.25 (18-58)	MW	0.19
LVIDs (mm)	24 (20-31)	25 (21-31)	MW	0.25
LVIDd (mm)	40 (32-48)	41.5 (35-48)	MW	0.133
LV-EF (%)	67 (61-72)	67 (63-74)	MW	0.619
LV-FS (%)	38 (32-42)	38 (35-45)	MW	0.55
Spirometry				
FVC *	94 (84-102)	92.5 (79-98)	MW	0.1
FEV1*	82 (70-94)	89 (80-96)	MW	<0.001*
FEV1/FVC	0.88 (0.7-1)	0.96 (0.85-1)	MW	<0.001*

BMI: Body mass index, HR: Heart rate, RR: Respiratory rate, BP: Bloof pressure, LAD: Left atrial diameter, LVIDs: Left ventricular internal diameter in systole, LVIDd: Left ventricular internal diameter in diastole, EF: Ejection fraction, FS: Fractional shortening, MW: Mann-Whitney U test, t: Independent samples t-test. FEV1: Forced expiratory volume in the 1st second, * Percentage predicted to normal values, FVC: Forced vital capacity.

Table-2: Comparison between the groups regarding conventional echocardiographic parameters of the right ventricle.

Parameter	Patients (n=60)	Control (n=60)	test	*p-value*
ESPAP mmHg	21 (17-26)	20 (15-25)	MW	0.057
RV wall thickness (cm)	0.33±0.045	0.32±0.04	t	0.058
RVEDD (cm)	2.75 (1-3.5)	2.4 (0.9-3.5)	MW	0.046
Tricuspid peak E velocity(cm/sec.)	86.5±8	87±9.3	t	0.64
Tricuspid peak A velocity(cm/sec.)	66.5 (35-87)	65 (39-87)	MW	0.69
Tricuspid peak E/A ratio	27 (16-55)	33 (18-58)	MW	0.001
TAPSE (cm)	2 (1.8-2.5)	2 (1.7-2.4)	MW	0.112
Main Pulmonary A. Diameter(cm)	1.98±0.3	1.91±0.3	t	0.209

ESPAP: Estimated systolic pulmonary artery pressure, RV: Right ventricle, RVEDD: Right ventricular end diastolic diameter, TAPSE: Tricuspid annular plane systolic excursion, MW: Mann-Whitney U test, t: Independent samples t-test.

Table-3: Comparison between the groups regarding Tissue Doppler echocardiographic parameters of the right ventricle.

Parameter	Patients (n=60)	Control (n=60)	test	*p-value*
Lateral tricuspid systolic S/ peak velocity (cm/sec)	11.7±1.34	12±1.23	t	0.336
Lateral tricuspid Ê	13.9±1.63	15.1±2.19	t	0.001
Lateral tricuspid late diastolic Â peak velocity (cm/sec)	10.35 (8-14.5)	11 (8-14.4)	MW	0.018

Continued on next page

Table-3: *continued from previous page*

Parameter	Patients (n=60)	Control (n=60)	test	*p-valuee*
Lateral Ê / Â ratio	1.34 (1-1.88)	1.35 (1-1.89)	MW	0.532
IVRT (m.sec)	48 (36-66)	39 (36-55)	MW	0.001
IVCT (m.sec)	52 (40-65)	46 (40-61)	MW	< 0.001
ET (m.sec)	239 (200-299)	214 (198-295)	MW	< 0.001
MPI (%)	0.42 (0.34-0.49)	0.39 (0.30-0.47)	MW	0.005

IVRT: Isovolumetric relaxation time, IVCT: Isovolumetric contraction time, ET: Ejection time, MPI: Myocardial performance index, MW: Mann-Whitney U test, t: Independent samples t-test.

Table-4: Relationship between the severity of asthma and Tissue Doppler indices of significant difference.

	Mean ±SD	Median (range)	test	*p-value*
Lat. Tricuspid velocity E\ (cm/s)				
Healthy	15.7 ± 2.1	15 (11-21)	owA	
Mild asthma	13.9 ± 1.6	14 (11-17)	9.55	0.004
Moderate asthma	13.8 ± 1.6	14 (11-17)		S
Isovolumetric relaxation time (IVRT) (m.sec)				
Healthy	41.3± 4.59	39 (36-55)	KW	
Mild asthma	46.3 ± 5	48 (36-56)	28.2	<0.001
Moderate asthma	48.3 ± 7.63	48.5 (36-66)		S
Isovolumetric contraction time (IVCT) (m.sec)				
Healthy	46.4 ± 5.2	46 (40-61)	KW	
Mild asthma	51.4 ± 6	53.5 (40-59)	23.9	<0.001
Moderate asthma	52.3 ± 5.9	52 (41-63)		S
Ejection time (ET) (m.sec)				
Healthy	220.3 ± 20.7	214 (198-295)	KW	
Mild asthma	238.8 ± 27.5	235 (200-286)	17.5	<0.001
Moderate asthma	243.6 ± 31.1	241 (202-299)		S
Myocardial performance index (MPI) (%)				
Healthy	0.39 ± 0.027	0.40 (0.30-0.47)	KW	
Mild asthma	0.41 ± 0.031	0.405(0.36-0.49)	9.4	0.009
Moderate asthma	0.41 ± 0.027	0.41 (0.34-46)		S

SD: Standard deviation, owA: One-way analysis of variance, KW: Kruskal Wallis test.

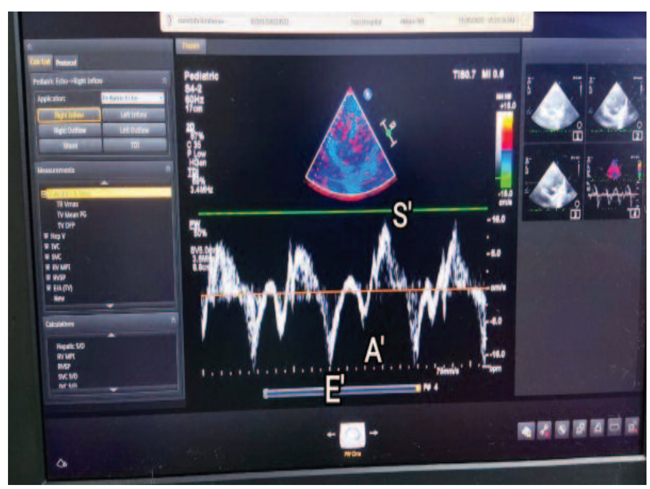

Figure 1: Tissue Doppler of right ventricle (RV), with the curser positioned in the lateral border of tricuspid annulus measuring two major negative velocities E` and A`. Major positive systolic velocity was recorded at S`.

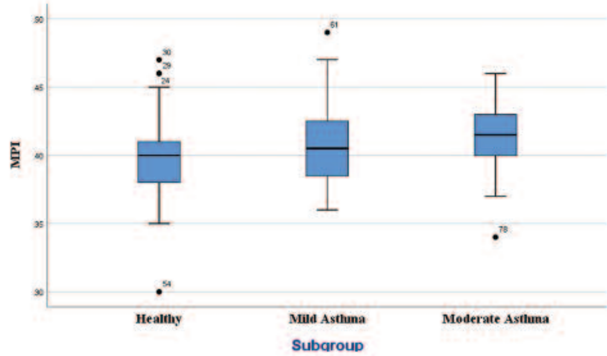

Figure 2: Box-plot distribution of myocardial performance index (MPI) among the subgroups.

Deterioration in TDE parameters increased with asthma severity (Table 4, Figure 2).

Discussion

Asthma is a chronic inflammatory disorder of the airways characterised by their hyper-reactivity to various stimuli that results in different symptoms. Bronchial asthma is common in children and has shown increasing prevalence and morbidity.

Asthmatic children in the current study were 55% males, which was consistent with literature[11]. Childhood asthma is common among males, while adult asthma is more common in females, and the reversal of prevalence during puberty suggests a role being played by sex hormones in asthma aetiology.

In the current study, cases and controls were not significantly different regarding gender, age, HR, RR and BP, which has been reported earlier as well.

The asthmatics in the current study aged 5-15 years, showing the highest point prevalence rate in age groups. Also, the current study found no significant difference between the groups regarding FVC, while there was highly significant difference regarding FEV1 and FEV1/FVC. This is in agreement with literature. Although a study[12] showed significant differences regarding FEV1 and FEV1/FVC between asthmatic and control groups, it contradicted the current findings, showing significant difference regarding FVC as well . A study did not use spirometry, and used the mini wright peak flow rate (PEFR) and chest X-ray (CXR).[5]

Echocardiographic findings in the current study are also in line with earlier studies.[5,12,14,15]

The current study showed RV dilatation rather than hypertrophy in asthmatic children compared to the controls. This was consistent with Abdelmohsen et al.[12], while Shedeed[5] showed RV hypertrophy. This may be explained by short duration of illness with normal estimated systolic pulmonary artery pressure and exclusion of severe asthma in the current study. A study[14] showed significant thickening of RV wall even in children with mild, well-controlled asthma with normal pulmonary function.

Main pulmonary artery diameter and estimated systolic pulmonary artery pressure showed no significant difference between the groups in the current study, which may be due to the short duration of illness and small age groups, and explains the absence of RV hypertrophy in the study. This disagrees with Abdelmohsen et al.[12]

There was no difference between the groups regarding tricuspid peak E velocity, tricuspid peak A velocity and E/A ratio in the current study. This was in agreement with Shedeed[5] and Ozdemir et al.[14]

TAPSE obtained from conventional M-Mode did not show a significant difference between the groups, which may suggest that RV systolic function was preserved in the current study.

The application of TDE was approved for clinical use in 2004. Whereas conventional Doppler can assess blood flow velocity by measuring signals of low amplitude and high velocity from fast-moving red blood cells (RBCs), using similar principles in TD to record shifts in ultrasonic frequencies from slowly moving tissue rather than fast-moving blood through different filters where these signals, which are of high amplitude and low velocity, can be recorded preferentially. It considers a powerful method for quantifying regional myocardial function.

In the current study, TDE showed lateral tricuspid systolic S\ velocity did not differ significantly between the groups. Lateral tricuspid early and late diastolic peak velocities (E\ and A\) were significantly lower in asthmatics. Similar results were reported by Abdelmohsen et al.[12] and Ozdemir et al.[14] Shedeed[5] showed lower lateral peak E\ and A\ in asthmatics as well, but lateral peak S\ was also lower, suggesting RV systolic affection.

IVRT of the RV was significantly longer in the cases than the controls, indicating that asthmatics had impaired relaxation pattern of the RV and consequently impaired RV diastolic function. This was in agreement with Ozdemir et al.[14] Also, Shedeed[5] showed that both IVRT and IVCT were prolonged in asthmatics.

MPI gained acceptance in assessing ventricular function and predicting clinical outcomes as it evaluates both ventricular diastolic and systolic functions.

The average RV MPI was significantly higher in asthmatics than the controls, reflecting global deterioration of myocardial performance in asthmatics. The subclinical impairment of RV function might be explained by attacks of hypoxaemia and pulmonary hypertension during asthma exacerbation which could challenge asthma diagnosis in children, especially intermittent asthma.[18] TD is angle-dependent and is affected by translational heart movement.[19]

The current study has limitations as the sample size was not calculated, which could influence the power of the study. Besides, the sample size was too small to allow generalisation of the findings.

Conclusion

TDE could detect subtle RV diastolic dysfunction in asthmatic children even with no clinical symptoms and normal findings on conventional echocardiography.

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Hough KP, Curtiss ML, Blain TJ, Liu RM, Trevor J, Deshane JS, et al. Airway Remodeling in Asthma. Front Med (Lausanne) 2020;7:e191. doi: 10.3389/fmed.2020.00191.
2. Chicherina EN, Malykh SZ, Shipitsina VV. The myocardial condition in chronic obstructive pulmonary disease and bronchial asthma. Klin Med (Mosk) 2007;85:23-6.
3. D'hooge J, Heimdal A, Jamal F, Kukulski T, Bijnens B, Rademakers F, et al. Regional strain and strain rate measurements by cardiac ultrasound: principles, implementation and limitations. Eur J Echocardiogr 2000;1:154-70. doi: 10.1053/euje.2000.0031.
4. Palka P, Lange A, Fleming AD, Fenn LN, Bouki KP, Shaw TR, et al. Age-related transmural peak mean velocities and peak velocity gradients by Doppler myocardial imaging in normal subjects. Eur Heart J 1996;17:940-50. doi: 10.1093/oxfordjournals.eurheartj.a014977
5. Shedeed SA. Right ventricular function in children with bronchial asthma: a tissue Doppler echocardiographic study. Pediatr Cardiol 2010;31:1008-15. doi: 10.1007/s00246-010-9753-2.
6. Global Initiative for Asthma (GINA). Global Strategy for Asthma Management and Prevention. [Online] 2022 [Cited 2022 March 11]. Available from URL: https://ginasthma.org/wp-content/uploads/2022/07/GINA-Main-Report-2022-FINAL-22-07-01-WMS.pdf
7. Georgy V, Fahim HI, El-Gaafary M, Walters S. Prevalence and socioeconomic associations of asthma and allergic rhinitis in northern [corrected] Africa. Eur Respir J 2006;28:756-62. doi: 10.1183/09031936.06.00089005.
8. Uluçay A, Tatli E. Myocardial performance index. Anadolu Kardiyol Derg 2008;8:143-8.
9. Buc M, Dzurilla M, Vrlik M, Bucova M. Immunopathogenesis of bronchial asthma. Arch Immunol Ther Exp 2009;57:331-44. doi: 10.1007/s00005-009-0039-4.
10. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. Allergy 2004;59:469-78. doi: 10.1111/j.1398-9995.2004.00526.x.
11. Dharmage SC, Perret JL, Custovic A. Epidemiology of Asthma in Children and Adults. Front Pediatr 2019;7:e246. doi: 10.3389/fped.2019.00246.
12. Abdelmohsen G, Mohamed H, Mohsen M, Abdelaziz O, Ahmed D, Abdelsalam M, et al. Evaluation of cardiac function in pediatric patients with mild to moderate bronchial asthma in the era of cardiac strain imaging. Pediatr Pulmonol 2019;54:1905-13. doi: 10.1002/ppul.24485.
13. American Lung Association. Trends in Current Asthma Rate by Age, Sex and Race/Ethnicity. [Online] 2022 [Cited 2022 March 11]. Available from URL: https://www.lung.org/research/trends-in-lung-disease/asthma-trends-brief/data-tables/trends-current-asthma-age-sex-race
14. Ozdemir O, Ceylan Y, Razi CH, Ceylan O, Andiran N. Assessment of ventricular functions by tissue Doppler echocardiography in children with asthma. Pediatr Cardiol 2013;34:553-9. doi: 10.1007/s00246-012-0493-3.
15. Ghandi Y, Habibi D, Abasi M. The Effect of Bronchial Asthma on Interatrial Electromechanical Delay Coupling Obtained Using Tissue Doppler Imaging. Iran J Med Sci 2019;44:196-203
16. Ho CY, Solomon SD. A clinician's guide to tissue Doppler imaging. Circulation 2006;113:e396-8. doi: 10.1161/CIRCULATIONAHA.105.579268.
17. Cheung MM, Smallhorn JF, Redington AN, Vogel M. The effects of changes in loading conditions and modulation of inotropic state on the myocardial performance index: comparison with conductance catheter measurements. Eur Heart J 2004;25:2238-42. doi: 10.1016/j.ehj.2004.07.034.
18. Vogelberg C. Preschool children with persistent asthmatic symptoms. Ther Clin Risk Manag 2019;15:451-60. doi: 10.2147/TCRM.S170979.
19. Kukulski T, Hübbert L, Arnold M, Wranne B, Hatle L, Sutherland GR. Normal regional right ventricular function and its change with age: a Doppler myocardial imaging study. J Am Soc Echocardiogr 2000;13:194-204. doi: 10.1067/mje.2000.103106.