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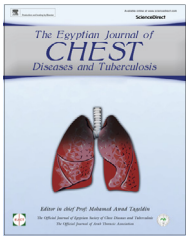

ORIGINAL ARTICLE

Right ventricular diastolic dysfunction in asthmatic patients

K.E. Sobhy [a], R.I.M. El-Korashy [a,*], M.K. Ahmed [b], F.G.M. Fayed [c]

[a] *Faculty of Medicine, Cairo University, Egypt*
[b] *Faculty of Medicine, Menoufia University, Egypt*
[c] *Menoufia Chest Hospital, Egypt*

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KEYWORDS

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Abstract Asthmatic patients develop right heart affection from early stages through different mechanisms. The current study was performed aiming to assess the right ventricular diastolic dysfunction in different asthmatic stages. The study population was fifty persons subdivided into 30 asthmatic adults and 20 healthy control subjects.

Results showed that the prevalence of right ventricular dilatation was statistically higher among asthmatic adults (66%) than controls (0%). Also, there was a significant elevation of the mean value of ESPAP among asthmatic adults (24 ± 7.18) than the control group (17.8 ± 4.98) ($P < 0.05$). In addition the mean value of RVEDD was significantly higher among asthmatic adults (17.47 ± 4.51 cm) compared to control subjects (14.54 ± 3.15 cm) ($P < 0.05$). Also, a more deleterious effect was found that severe asthmatic cases suffered more impairment in diastolic functions of the right ventricle than mild and moderate cases, which means that patients with bronchial asthma have right ventricular diastolic dysfunction and the degree of this dysfunction is related to the severity of the disease.

Introduction

Obstructive lung diseases including asthma, present a significant burden on healthcare system [1]. Asthmatic patients develop right heart affection from early stages, in which hyperinflation of the lungs and high airway resistance can lead to substantial affection of the cardiac performance [2]. Right ventricular hypertrophy and dilatation are observed with increasing severity of asthma [3,4]. Also the occurrence of reported myocardial ischemia and cardiac arrhythmias in persistent asthma may play a role [5]. Autonomic dys-regulation with increased cardiac vagal activity occurs in bronchial asthma [6] leading to enhanced neural drive to the sino-atrial node [7]. The recurrent exposure to hypoxemia in recurrent asthmatic attacks may be one of the mechanisms which leads to substantial pulmonary vasoconstriction and narrowing of the pulmonary vasculature [8]. This may be due to increased endothelin ET-1 expression as was reported in acute exacerbation

* Corresponding author. Tel.: +20 1122299919; fax: +2 02 38371400.
E-mail address: rimkorashy@yahoo.com (R.I.M. El-Korashy).

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of asthma [9], this ET-1 has growth-promoting (myocardial cell hypertrophy) and possible cardiotoxic, arrhythmogenic properties and has been shown to be a potent predictor of cardiac death [10]. ET-1 also stimulates the release of aldosterone and catecholamines and promotes anti-natriuretic activity in the kidney [11]. B2-agonist administration leads to a shift of the ANS's sympathovagal balance towards sympathetic dominance with its positive chronotropic and positive inotropic effects. This shift is associated with increased cardiac mortality and morbidity and with an increased risk of sudden coronary death [12]. The assessment of right heart by echocardiography is important because the right ventricular function has been shown to be a major determinant of clinical outcome [13].

Aim of work

The aim of this work is to assess right ventricular diastolic dysfunction in different asthmatic stages.

Methodology

The study populations include 50 subjects divided into 30 asthmatic and 20 apparently healthy control subjects, age and sex matched.

The patients were selected after exclusion of:

Ischemic heart disease, cardiomyopathy, systemic hypertension, pericardial disease, smokers, acute exacerbations of asthma, primary and secondary valvular heart disease.

For all subjects: clinical history and examination, spirometer with pre and post bronchodilator measurements, echocardiography (conventional and tissue Doppler imaging) were done.

Results

Fifty adults were divided into 30 asthmatic patients sub-classified according to the GINA guidelines 2007 (Table 1), and 20 apparently healthy control subjects were enrolled in the study, age matched (control: 38.35 ± 8.49, cases: 38.17 ± 9.86) and sex (male:female ratio, control 7:13, cases 7:23) matched.

Discussion

The current study showed that the prevalence of right ventricular dilatation was statistically higher among asthmatic adults (66%) than control (0%). Also, with significant elevation of the mean value of ESPAP among asthmatic adults (24 ± 7.18) than the control group (17.8 ± 4.98) ($P < 0.05$) as shown in Table 2. In addition the mean value of RVEDD was significantly higher among asthmatic adults (17.47 ± 4.51 cm) compared to control subjects (14.54 ± 3.15 cm) ($P < 0.05$) (Table 2), which was in agreement with the results of other clinical studies [14–16]. This may be explained by increased negative pressure during inspiration and positive pressure during active expiration leads to large swings in intrathoracic pressure and exaggeration of the normal cyclic changes in right ventricular preload and afterload. These markedly negative swings may also contribute to increases in PAP and increases in venous return to the right heart with subsequent right ventricular dilation [14], leading to increase in the stroke volume [17]. This is expressed experimentally, by the U shaped relation between vascular resistance and lung volume, and therefore, in normal respiratory conditions, lung inflation is expected to have little or no effect on vascular resistance [18].

Table 1 Distribution of asthma severity in cases.

		Cases ($n = 30$)
Asthma severity	Mild	9 (30%)
	Moderate	17 (56.7%)
	Severe	4 (13.3%)

This was proved on clinical bases by a study carried by Jardin et al., on 7 asthmatic patients during an acute attack, using simultaneous bedside right heart catheterization and conventional echocardiography. The study revealed a significant increase in the right ventricular area at both end-systole and end-diastole during inspiration [17].

Another study evaluated 89 asthmatic patients using echocardiography. It was established that, such patients had increased pressure in the pulmonary artery (Table 2), as well as diastolic dysfunction (Table 4). These changes correlate with the degree of severity of BA, on the contrary to the current study (Table 3) [19].

TDI can allow quantification of regional and local myocardial velocities, with less dependence on the chamber geometry [20], the Doppler principles are used to quantify the higher amplitude, lower velocity signals of the myocardial tissue motion and measure the myocardial tissue motion and velocity thus enables the echocardiographer to quantify regional and global systolic and diastolic functions of both ventricles [21]. Thus it was further used in the current study to assess the right ventricular parameters.

The right ventricle completes the diastolic period in four phases: isovolumetric relaxation (IVR), rapid filling phase (E'), slow filling phase (A') and atrial contraction [22].

The results shown in Table 4 regarding the E', A' and E'/A' ratio of the free right ventricle wall and septal wall, and the IVRT in the cases and control group as measured by TDI, means that adult asthmatics had impaired relaxation pattern of the right ventricle and consequently impaired right ventricular diastolic function. These results were in agreement with different clinical studies, in which by using, TDI of right ventricular diastolic function, the peak E' velocity (10.08 ± 2.8 cm/s) among studied asthmatic cases was significantly lower than controls (12.4 ± 2.3 cm/s), while IVRT (128.9 ± 30.7 ms) of the right ventricular free wall was significantly higher among cases than controls (91.1 ± 32.6 ms)[15].

And in another study, it was found that the peak E' velocity and E'/A' ratio (13.6 ± 4.1 cm/s, 1.2 ± 0.4) among mild cases were significantly lower than controls (15.9 ± 4.0 cm/s, 1.5 ± 0.4) respectively ($p < 0.001$), while the mean value peak A′ velocity and IVRT (11.5 ± 4.0 m/s, 70.9 ± 6.1 ms) of the right ventricular free wall were significantly higher among mild cases than controls (10.4 ± 3.9 m/s, 55.3 ± 6.8 ms) respectively ($p < 0.001$) [23].

Also, more deleterious effect was found, that severe asthmatic cases suffered more impairment in diastolic functions of the right ventricle than mild and moderate cases (Table 5), which means that patients with bronchial asthma have right ventricular diastolic dysfunction and the degree of this dysfunction is parallel with the severity of the disease.

Table 2 Conventional echo parameters in cases and control.

Conventional echo		Control ($n = 20$)	Cases ($n = 30$)	t test	p-Value
		$\chi^- \pm$ SD	$\chi^- \pm$ SD		
RVEDD (cm^2)		14.54 ± 3.15	17.47 ± 4.51	2.52	0.05
RT ventricle dilatation	No	20 (100%)	20 (66.7%)	8.33*	0.004
	Yes	0 (0%)	10 (33.3%)		
EPASP (mmHg)		17.8 ± 4.98	24 ± 7.18	3.36	0.002

RVEDD: right ventricular end diastolic diameter: normal range: up to 18 + 5.
EPASP: estimated pulmonary artery systolic pressure: normal range.
* Chi-square test (χ^2).

Table 3 Conventional echocardiographic findings of RV and asthma severity.

Severity of asthma	Mild (No = 9)	Moderate (No = 17)	Severe (No = 4)	ANOVA test	P-Value
	$\chi^- \pm$ SD	$\chi^- \pm$ SD	$\chi^- \pm$ SD		
EPASP	65.67 ± 3.43	65.94 ± 5.13	66.75 ± 4.19	0.88	0.43

Table 4 TDI right ventricular diastolic parameters.

Right ventricle		Control ($n = 20$)	Cases ($n = 30$)	t test	P-Value
		$\chi^- \pm$ SD	$\chi^- \pm$ SD		
Free wall	E' (cm/s)	12.3 ± 2.29	10.27 ± 2.73	2.75	0.008
	A' (cm/s)	11.5 ± 3.86	13.2 ± 3.17	1.7	0.09
	E'/A'	1.17 ± 0.37	0.83 ± 0.35	3.17*	0.002
	IVRT (ms)	44.7 ± 11.23	78.37 ± 17.84	7.49	< 0.001
Septal wall	E'	10.55 ± 2.1	9.2 ± 2.16	2.23	0.03
	A'	8.3 ± 1.59	9.47 ± 2.18	2.06	0.04
	E'/A'	1.32 ± 0.36	1.04 ± 0.4	2.46*	0.01
	IVR	68.45 ± 10.89	79.83 ± 13.49	3.15	0.003

E' early diastolic myocardial relaxation velocity (early rapid filling phase).
A' myocardial velocity associated with atrial contraction (late active filling phase).
IVRT: isovolumetric relaxation time.
* Mann Whitney test.

Table 5 Correlation between TDI findings of the right ventricular and asthma severity.

	Severity of asthma	Mild (No = 9)	Moderate (No = 17)	Severe (No = 4)	ANOVA test	P-Value
		$\chi^- \pm$ SD	$\chi^- \pm$ SD	$\chi^- \pm$ SD		
Free wall	E'	10.67 ± 2.83	10.12 ± 2.98	10.0 ± 1.63	0.13	0.88
	A'	13.67 ± 3.46	12.59 ± 3.29	14.75 ± 0.96	0.89	0.42
	E'/A'	085 ± 0.41	0.86 ± 0.35	0.68 ± 0.09	0.48	0.63
	IVR	80.67 ± 13.02	74.82 ± 21.11	88.25 ± 5.38	1.03	0.37
Septal wall	E'	9.33 ± 1.8	9.29 ± 2.37	8.5 ± 2.38	0.23	0.79
	A'	10.0 ± 2.18	9.06 ± 2.38	10.0 ± 0.82	0.67	0.52
	E'/A'	0.98 ± 0.3	1.12 ± 0.46	0.87 ± 0.31	0.99*	0.61
	IVR	83.22 ± 7.21	81.18 ± 16.19	70.75 ± 8.66	1.22	0.31

* Kruskal Wallis test.

This was in agreement with the finding reported by Shedeed, which showed that values of right ventricular free wall peak E' velocity, peak A' velocity, E'/A' ratio and IVRT (7.89 ± 1.08 cm/s, 4.33 ± 1.28 cm/s, 2.04 ± 0.82, 160.3 ± 8.39 ms) respectively were significantly different when compared to their values among mild (12.50 ± 1.62 cm/s, 6.82 ± 1.36 cm/s, 1.69 ± 0.26, 99.41 ± 8.20 ms) and moderate asthmatics (8.80 ± 2.35 cm/s, 5.43 ± 1.93 cm/s, 1.83 ± 0.47, 162.9 ± 7.43, 7.63 ± 1.20 ms) respectively ($P < 0.01$) [15].

Summary and conclusion

Asthmatic adults have right ventricular affection in the form of diastolic dysfunction starts early in the disease. Conventional and tissue Doppler echocardiography should be performed for asthmatic patients to assess the progress of the disease process.

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