Assessment of the relation between pulmonary hypertension severity and left ventricular diastolic dysfunction in patients with ischemic heart disease

Mahmoud Shawky Abd-El moneum

Cardiology Department, Benha University Hospital, Benha city, Egypt.

Author

Mahmoud Shawky Abd-El moneum, M.D., Cardiology Department, Benha University Hospital, Benha city, Egypt.

Background. *Association between pulmonary hypertension and left ventricular (L.V.) diastolic dysfunction in patients with ischemic heart disease has been observed. However, the relation between the severity of pulmonary hypertension and left ventricular diastolic dysfunction is still unclear.*

Objectives. *To explore the relationship between pulmonary hypertension severity and L.V. diastolic dysfunction in patients with ischemic heart disease.*

Patients and methods. *200 symptomatic patients with ischemic heart disease were included in this study. History taking, clinical examination, and echocardiography were performed to all patients, LV dimensions, systolic and diastolic function, and systolic pulmonary artery pressure (SPAP) were measured. We characterized the patients into two groups as indicated by the presence or absence of diastolic dysfunction.*

Results. *Patients with diastolic dysfunction had significantly higher SPAP ($p < 0.00001$), and significantly higher incidence of severe pulmonary hypertension ($p = 0.034$). Autonomous indicators for the presence of severe pulmonary hypertension were E/E\ > 15, E/A< 1 and E-wave DT < 160.*

Conclusion. *patients with ischemic heart disease in addition to left ventricular diastolic dysfunction had a higher systolic pulmonary artery pressure and a higher incidence of severe pulmonary hypertension. Systolic pulmonary artery pressure was essentially connected with LV diastolic dysfunction.*

Key Words: *left ventricular diastolic dysfunction, pulmonary hypertension.*

* Corresponding author. Tel.: +2001223723050. E-mail: Mahmoudshawky206@gmail.com

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Introduction

Elevated pulmonary artery pressure in patients with ischemic heart disease has been observed a long time ago. Oliver and his partners in 1978 have discovered a relationship between the increase in both pulmonary artery pressure and ischemic heart disease [1]. LV diastolic dysfunction however are at increased risk of developing heart failure [2] and it is seen that the incidence of heart failure with preserved ejection fraction (HFpEF) is particularly higher among ischemic patients [3–4]. When present in ischemic patients with diastolic dysfunction and/or HFpEF, pulmonary hypertension has a deleterious effect on mortality and morbidity [5]. Beside the presence of diastolic dysfunction, other factors were found to be associated with the presence of pulmonary hypertension in patients with ischemic heart disease like elevated pulmonary vascular resistance, declined renal function, and increased pro-Brain Type Natriuretic Peptide (pro-BNP) levels [6]. However, the severity of pulmonary hypertension in patients with ischemic heart disease and its relation to different indices of diastolic function has not been yet studied. Along these lines, the point of this work was to investigate the relationship between pulmonary hypertension severity and different indices of LV diastolic function in patients with ischemic heart disease.

Patients and methods

This study was performed in the Cardiology Department, Benha University during the period from January 2017 till November 2018. This study included 200 symptomatic patients with ischemic heart disease.

Patients were barred from this study if one or more of the following were present:

- Severe pulmonary disease «identified as forced vital capacity < 50 %» [7–9].
- LV systolic dysfunction with ejection fraction (EF) <50 %.
- Known hypertension.
- More than mild aortic or pulmonary stenosis, mitral or aortic regurgitation > grade 2, or severe tricuspid regurgitation.
- Significant congenital heart disease that may affect pulmonary pressure.
- Atrial fibrillation.

We made the following to every patient after obtaining a written informed consent:

1) History taking and clinical examination.

2) Pulmonary function test with measuring of forced vital capacity for exclusion.

3) Echocardiography: Standard transthoracic echocardiographic and Doppler studies were performed for all patients using GE VIVID E9 machine with 2.5 MHz transducers. The following measures were taken:

- M-mode measures: Left atrial (LA) diameter, left ventricular end diastolic (LVEDD) and systolic dimensions (LVESD), ejection fraction (EF) and fraction of shortening (FS).
- Left atrial volume (LAV) was determined by measuring LA area in apical four, and apical two chamber views.
- Mitral valve (MV) flow velocities by pulsed Doppler; E-wave, A-wave E/A ratio and E-wave deceleration time (DT).
- Tissue Doppler of the septal segment of MV annulus was done from the apical 4 chamber view with measuring of the peak systolic wave ($S^{\backslash}$), early ($E^{\backslash}$), late diastolic waves (A) and $E/E^{\backslash}$ were calculated.
- Diastolic function was evaluated by combining all measured parameters. The diastolic function was considered normal if E/A > 1, DT between 160 and 240 ms, E/A > 1, and $E/E^{\backslash} < 15$.
- Grade 1 diastolic dysfunction (impaired relaxation pattern) was diagnosed when E/A < 1, and DT > 240 ms, plus either E/A < 1, or $E/E^{\backslash} <8$.
- Grade 2 diastolic dysfunction (pseudo normal pattern) was diagnosed when E/A between 1 and 2, and DT between 160 and 240 ms, plus either E/A < 1, or $E/E^{\backslash}$ 8–15.
- Grade 3 diastolic dysfunction (restrictive filling pattern) was diagnosed when E/A > 2, and DT < 160 ms, plus either E/A < 1, or $E/E^{\backslash} > 15$ [10–11].
- As all our patients had mild or moderate tricuspid regurgitation, systolic pulmonary artery pressure (SPAP) was calculated from the peak continuous wave Doppler signal of tricuspid regurgitant jet velocity and adding a constant value for right atrial pressure to it (10 mmHg). Patients with SPAP > 40 mmHg

were considered as having pulmonary hypertension, and patients with SPAP > 80 mmHg were considered as having severe pulmonary hypertension [12].

4) Statistical analysis: All data were analyzed using the SPSS for Windows package program (Version 20.0; Armonk, NY, USA:IBM Corp.). Differences between patients' group and control group were analyzed using x^2 test and Student's t-test. Relationsships between different variables were investigated by Pearson correlation analysis. The logistic regression analysis was evaluated by the Hosmer–Lemeshow goodness-of-fit test.p value < 0.05 was regarded as being statistically significant. We repeated the echocardiographic measures in 30 patients within 7 days from the first measure for assessing the intraobserver variability. The interobserver and intraobserver variability were calculated by dividing the difference between the two sets of measurements, by the mean of the two observations.

Results

Patients were divided into two groups as indicated by the presence or absence of LV diastolic dysfunction:

Group 1: Included 100 patients without diastolic dysfunction.

Group 2: Included 100 patients with diastolic dysfunction.

There was no significant difference between the two groups regarding clinical data of the two groups as the mean age of patients in group A was 54.46± 7.55 years and the mean age of patients in group B was 55.02 ± 6.80 years (p-value = 0.582), and regarding sex distribution, 57% of patients in group A were males and 43% of the same group were females and group B included males constituting 55% of the group and females representing 45% of the group (p-value=0.776), the mean value of BMI in group A was 26.22 ± 1.82 and was 28.86 ± 1.82 and in group B (p-value= 0.325), hypertension was in 60% of patients in group A and 51% of patients in group B (pvalue=0.200), also diabetes mellitus was in 53% of patients in group A and 50% of patients in group B (p-value=0.671), 43 patients in group A were smoker and 42 smoker were in group B (p-value=0.9), and dyslipidemia was in 37% of patients in group A versus 40% of patients in group B (p-value=0.7) (Table 1).

As shown in Table 2, patients with diastolic dysfunction had significantly higher LA diameter (31.1 ±5.8 mm in group 1, versus 33.8 ± 4.9 mm in group 2, p = 0.013), higher LAV (36.2 ± 8.61 ml in group 1, versus 42.1 ±9.64 ml in group2, p = 0.0011), lower septal E\ velocity (11.3 ± 3.58 cm/s in group 1, versus 8.1 ±4.87 cm/s in group 2, p = 0.0071), higher septal E/E\ ratio (9.7 ± 3.11 in group 1, versus 14.2 ± 4.65 in group 2, p < 0.00001), higher SPAP (25.3 ± 7.12 mmHg in group 1, versus 33.4 ±14.34 mmHg in group 2, p < 0.00001), and significantly higher incidence of severe pulmonary hypertension (0% in group 1, versus 7%, p = 0.034). There was no significant difference

Table 1. **Comparison of clinical data among studied groups**

		Group A	Group B	p. value
Age (years)	Mean ± S. D	54.46 ± 7.55	55.02 ± 6.80	0.582
BMI	Mean ± S. D	26.22 ± 1.82	28.86 ± 1.82	0.325
Sex	Male (%)	57 (57%)	55 (55%)	0.776
	Female (%)	43 (43%)	45 (45%)	
HTN	+ve	60	51	0.200
		60.0%	51%	
	- ve	40	49	
		40.0%	49%	
DM	+ve	53	50	0.671
		53%	50.0%	
	- ve	47	50	
		47%	50.0%	
Smoking	+ve	43	42	0.9
		43.0%	42.0%	
	- ve	57	58	
		57.0%	58.0%	
Hyperlipidemia	+ve	37	40	0.7
		37.0%	40.0%	
	- ve	63	60	
		63.0%	60.0%	

Table 2. **Comparison of echocardiographic data among studied groups**

	Group A	Group B	p. value
LAD (mm)	31.1 ± 5.8	33.8 ± 49	0.013
LAV (ml)	36.2 ± 8.61	42.1 ± 9.64	0.0011
Septal E\ (cm/s)	11.3 ± 3.58	8.1 ± 4.87	0.007
Septal E/E\	9.7 ± 3.11	14.2 ± 4.65	0.00001
LVEDD (mm)	46.8 ± 7.82	48.2 ± 9.17	0.408
LVESD (mm)	31.3±6.51	33.4 ± 7.23	0.116
FS (%)	32.4 ± 7.42	30.1 ± 8.16	0.129
EF (%)	62.40 ± 6.95	62.16 ± 7.01	0.808
SPAP (mmHg)	25.3 ± 7.12	33.4 ± 14.34	<0.00001
severe pulmonary hypertension	0 (0%)	7 (10%)	0.034

LAD = left atrial dimension, LAV = left atrial volume, LAV = left atrial volume index, septal E\: the early diastolic tissue Doppler wave of septal segment of mitral annulus, E: the early diastolic Doppler wave of mitral valve flow, LVEDD = left ventricular end diastolic dimension, LVESD = left ventricular end systolic dimension, FS = fraction of shortening, EF = ejection fraction, SPAP = systolic pulmonary artery pressure.

between the two study groups regarding other echocardiographic data.

Discussion

This study furnishes a complete correlation between patients with ischemic heart disease with and without diastolic dysfunction regarding the prevalence and severity of pulmonary hypertension. Left atrial diameter was seen to be higher in patients with diastolic dysfunction compared to those without. This was concordant with Mukherjee and his partners who defined two groups of patients with ischemic heart disease as indicated by presence or absence of pulmonary hypertension. They discovered that left atrial area was larger among ischemic heart patients with PH. This perception, bolster the idea that ischemic heart disease leads to both pulmonary venous as well as arterial hypertension. This can be demonstrated through the mechanism of pulmonary remodeling and increase pulmonary vascular resistance [6].

Furthermore Gerdts et al. in 2002 studied LA indices in patients with ischemic heart disease and sealed that patients with LA enlargement were older, more obese, had elevated systolic blood pressure and pulse pressure. Regarding indices of LV diastolic function, our results disclosed that a restrictive pattern obtained by E/E\> 15 was the strongest predictor of the presence of pulmonary hypertension this was followed by E/A < 1, and E-wave DT < 160 ms [13].

The prognostic importance of a restrictive filling pattern after acute myocardial infarction (AMI) was initially declared by Oh et al.in 1992 [14]. They considered the prognostic ramifications of this pattern in post AMI patients in a cohort of 62 patients. They discovered that restrictive filling pattern was related to a high occurrence of in-hospital congestive heart failure.

This was confirmed by Poulsen et al. in an age-selected population with a first AMI in which Doppler echocardiography was done within 1 hour of hospital admission and they found that deceleration of E-wave of MV flow < 130 ms was able to identify patients at risk of development of congestive heart failure following AMI [15].

In 1997, Nijland et al. declared in a study of 95 patients with first AMI that DT < 140 ms was related to a 22 % survival rate at 3 years compared with 100 % in the nonrestrictive group [16].

Although the study was limited by a small number of deaths, this finding has subsequently been confirmed in several studies [17–20].

In these studies, patients with a restrictive filling pattern have been characterized by higher age, more advanced LV systolic dysfunction, and a high risk of in-hospital heart failure.

The relation between ischemic heart disease and pulmonary hypertension was a matter of concern a long time ago, [1] but the debate continues about the exact mechanism of this relationship. However, the association of diastolic dysfunction and increased pulmonary resistance with pulmonary hypertension in patients with ischemic heart disease aroused the attention about their possible mechanism in the development of pulmonary hypertension in these patients [6].

The results support the relationship between LV diastolic dysfunction and pulmonary hypertension in patients with ischemic heart disease as we have found that severe pulmonary hypertension was more prevalent among with ischemic heart patients with diastolic dysfunction (10 % of patients with diastolic dysfunction had severe pulmonary hypertension versus 0 % of patients without). Also we have discovered that LV diastolic dysfunction indices (E/E\) ratio, E/A ratio, and (E-wave DT) were significantly correlated with SPAP.

Conclusion

- Ischemic heart patients with diastolic dysfunction had an elevated systolic pulmonary artery pressure and a higher incidence of severe pulmonary hypertension.
- Systolic pulmonary artery pressure was significantly correlated with different indices of LV diastolic function. — In patients with ischemic heart disease, E/E\ > 15, E/A 0 < 1, E-wave DT < 160 ms were independent predictors for pulmonary hypertension.
- Looking for pulmonary hypertension in patients with ischemic heart disease, currently when associated with LV diastolic dysfunction, may help in managing them and in predicting their prognosis.

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