Research Article

Assessment of The Relation Between Pulmonary Hypertension Severity and Left Ventricular Diastolic Dysfunction in Patients with Ischemic Heart Disease

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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 colleagues in 1978 have found an association 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 increased pulmonary vascular resistance, reduced renal function, and higher 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. So, the aim of our work was to explore the relationship between pulmonary hypertension severity and different indices of LV diastolic function in patients with ischemic heart disease.

Patients and methods

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

Patients were excluded from our study if one or more of the following were present:

- 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

- Severe pulmonary disease "identified as forced vital capacity< 50%" (7-9).

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 GEVIVID E9 machine with 2.5 MHz transducers. The studies were performed by two operators who were unaware of the patients 'clinical data or each other's measurements. 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 calculated 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\), early (E\), late diastolic waves (A) and E/E\ were calculated.

- Diastolic function was assessed 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\<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\<8.

- Grade 2 diastolic dysfunction (pseudo normal pattern) was diagnosed when E/A between 1 and 2, and DT between 160and 240 ms, plus either E/A < 1, or E/E\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\> 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 regurgitate 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. Correlations between different variables were investigated by Pearson correlation analysis. The logistic regression analysis was evaluated by the Hosmer–Leme show 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 intra observer variability. The inter observer and intra observer 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 according to 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 was28.86 ±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 (p-value=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 smokers 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).

		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 1: Comparison of clinical data among studied groups.

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 group 2, 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 between the two study groups regarding other echocardiographic data.

	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.		

Table 2: Comparison of echocardiographic data among studied groups.

Discussion

The present study provides a comprehensive comparison 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 colleagues who defined two groups of patients with ischemic heart disease according to presence or absence of pulmonary hypertension. They found that left atrial area was larger among ischemic heart patients with PH. This observation, support the concept that ischemic heart disease results in both pulmonary venous as well as arterial hypertension. This can be explained through the mechanism of pulmonary remodeling and increase pulmonary vascular resistance [6].

Furthermore, Gerdts et al. in 2002 studied LA indices inpatients with ischemic heart disease and concluded that patients with LA enlargement were older, were more obese, had higher systolic blood pressure and pulse pressure [7-12]. Regarding indices of LV diastolic function, our results revealed that a restrictive pattern denoted by that 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 reported by Oh et al. in 1992 [14]. They studied the prognostic implication of this pattern in post AMI patients in a cohort of 62 patients. They found that restrictive filling pattern was associated with 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 performed within 1 hour of hospital admission and they found that deceleration of E-wave of MV flow < 130 ms was capable of identifying patients at risk of development of congestive heart failure following AMI [15]. In 1997, Nijland et al. reported in a study of 95 patients with first AMI that DT < 140 ms was associated with 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].

Our 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 found also 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 a higher 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/A0 < 1, E-wave DT < 160 ms were independent predictors for pulmonary hypertension.

- Searching for pulmonary hypertension in patients with ischemic heart disease, especially when associated with LV diastolic dysfunction, may help in managing them and in predicting their prognosis.

Conflicts of interest

The authors have none to declare.

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