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Original Article

Correlation between pulmonary hypertension severity and left ventricular diastolic function indices in hypertensive patients

El-Shaimaa Seaoud, Mohammad M. Al-Daydamony*

Cardiology Department, Faculty of Medicine, Zagazig University, Egypt

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ABSTRACT

Background: Association between pulmonary hypertension and left ventricular diastolic dysfunction in hypertensive patients has been observed. However, the relation between the severity of pulmonary hypertension and different indices of diastolic dysfunction is still unclear.
Objectives: To explore the relationship between pulmonary hypertension severity and different indices of LV diastolic dysfunction in hypertensive patients.
Patients and methods: 112 asymptomatic hypertensive patients were included in our study. History taking, clinical examination, and echocardiography were done to all patients, LV dimensions, systolic and diastolic function, and systolic pulmonary artery pressure (SPAP) were measured. We classified the patients into two groups according to 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 ($p = 0.034$). There was a significant positive correlation between SPAP and E/E′ ratio ($r = 0.354$, $p = 0.00013$), and between SPAP and systolic blood pressure ($r = 0.231$, $p = 0.231$), and a significant negative correlation between SPAP and E′/A′ ratio ($r = -0.289$, $p = 0.0019$), and between SPAP and E-wave DT ($r = -0.265$, $p = 0.0047$). Independent predictors for the presence of severe pulmonary hypertension were E/E′ > 15, E′/A′ < 1, and E-wave DT < 160.
Conclusion: Hypertensive 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 of LV diastolic dysfunction indices.

1. Introduction

Elevated pulmonary artery pressure in hypertensive patients has been observed a long time ago. Oliver and his colleagues in 1978[1] have found an association between the increase in both pulmonary and systemic blood pressures.

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 hypertensive patients.[3]

When present in hypertensive 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 hypertensive patients 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 hypertensive patients 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 hypertensive patients.

2. Patients and methods

Our study was performed in the Cardiology Department, Zagazig University during the period from January 2015 till November 2016. The study included 112 asymptomatic hypertensive patients. We had defined hypertension according to the report of the Seventh Report of the Joint National Committee on High Blood Pressure "JNC 7" as systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg and or continuous use of antihypertensive drugs.[7] Poorly controlled hypertension was defined when systolic blood pressure ≥ 140 mmHg for patients

* Corresponding author.
E-mail address: m_daydamony@hotmail.com (M.M. Al-Daydamony).

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< 60 years or ≥150 mmHg for patients ≥ 60 years, or diastolic blood pressure ≥ 90 mmHg.[8]

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

- Severe pulmonary disease "identified as forced vital capacity < 50%".[9]
- LV systolic dysfunction with ejection fraction (EF) < 50%.
- Known coronary artery disease.
- 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.

Our Institutional Review Board had approved the study protocol. 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 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), fraction of shortening (FS), left ventricular mass (LVM), and mass index (LVMI) were obtained by two-dimensional guided M-mode from the left parasternal long axis view. Left ventricular hypertrophy was defined as LVMI ≥ 95 g/m^2 in women and 115 g/m^2 in men.[10]
   - Left atrial volume (LAV) was calculated by measuring LA area in apical four, and apical two chamber views. Left atrial volume index (LAVI) was calculated by dividing LAV on body surface area.
   - Mitral valve (MV) flow velocities by pulsed Doppler; E-wave, A-wave E/A ratio, E-wave deceleration time (DT), and isovolumetric relaxation time (IVRT).
   - 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′), and late diastolic waves (A′). E′/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 160 and 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.[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 χ^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–Lemeshow goodness-of-fit test. A 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 interobserver and intraobserver variability were calculated by dividing the difference between the two sets of measurements, by the mean of the two observations.

3. Results

Patients were divided into two groups according to the presence or absence of LV diastolic dysfunction:

Group 1: Included patients without diastolic dysfunction. This group included 42 patients, 27 males and 15 females; their mean age was 49.7 ± 11.75 years.

Group 2: Included patients with diastolic dysfunction. This group included 70 patients, 44 males and 26 females; their mean age was 53.2 ± 12.32 years.

As shown in Table 1, 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, $p = 0.0011$), higher LAVI (18.4 ± 5.32 ml/m^2 in group 1, versus 22.1 ± 6.55 ml/m^2 in group 2, $p = 0.0015$), 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 clinical or echocardiographic data.

As shown in Table 2, there was a significant positive correlation between SPAP and E/E′ ratio ($r = 0.354$, $p = 0.00013$), and between SPAP and systolic blood pressure ($r = 0.231$, $p = 0.014$). Also, there was a significant negative correlation between SPAP and E′/A′ ratio ($r = -0.289$, $p = 0.0019$), and between SPAP and E-wave DT ($r = -0.265$, $p = 0.0047$).

Regression analysis of the relation of different parameters to the presence of severe pulmonary hypertension is shown in Table 3. The independent predictors for the presence of severe pulmonary hypertension in the order of significance were E/E′ > 15 (OR = 5.69, CI = 3.96–7.42, $p = 0.0034$), E′/A′ < 1 (OR = 5.14, CI = 3.72–6.56, $p = 0.0094$), and E-wave DT < 160 ms (OR = 4.87, CI = 3.53–6.21, $p = 0.031$).

Inter- and intraobserver variability for different echocardiographic parameters ranged from 2.4 to 9.1%. For SPAP, inter- and intraobserver variability were 5.7 ± 2.3% and 6.9 ± 3.1% respectively.

4. Discussion

The present study provides a comprehensive comparison between hypertensive patients 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[6] who defined