Introduction

Heart failure is one of the most common causes of cardiovascular morbidity and mortality.1 About 60% to 70% of patients presenting with symptoms of heart failure have left ventricular (LV) systolic dysfunction. In the remaining patients who have preserved LV ejection fraction (LVEF), diastolic dysfunction is considered the main pathogenesis.1

Ventricular diastolic function involves relaxation and compliance phases.2 During relaxation, there is a loss of ventricular contraction without an increase in ventricular volume [denoted as iso-volumetric relaxation time (IVRT)]. This is followed by ventricular filling which results in an increase in pressure and volume of the ventricle. This phase is dependent on the compliance and stiffness of the ventricle.

Therefore, any pathological processes that impair the capacity of the LV to fill or increase the resistance to ventricular filling will lead to increased LV end-diastolic and pulmonary capillary wedge pressures leading to pulmonary congestion.2

Diastolic dysfunction is known to be associated with long-standing hypertension especially in the presence of left ventricular hypertrophy (LVH).1 Impaired myocardial relaxation and increased resistance to ventricular inflow results in left ventricular stiffness. Diastolic dysfunction is often seen in hypertrophic cardiomyopathy, elderly, aortic stenosis and myocardial infiltration example by amyloid.4 Diastolic heart failure is associated with a lower mortality rate compared to systolic dysfunction heart failure. However, it is associated with a high morbidity.5

Abstract

Introduction: The prevalence and severity of diastolic dysfunction (DD) among newly diagnosed hypertensives (NDHT) is not fully established. The aim of this study was to evaluate left ventricular diastolic function (LVDF) in patients with NDHT. Materials and Methods: This study involved 396 subjects (198 NDHT, age and gender matched 198 normotensives; age, 30 to 50 years). Parameters of LVDF included Doppler-echocardiographic measurements of peak early (E) and late (A) diastolic velocities, E-wave deceleration time (DT) and isovolumetric relaxation time (IVRT). E/A ratio of <1 was taken as an indication of DD. Results: Patients with NDHT had reduced E/A ratio (1.27 ± 0.41 vs 1.37 ± 0.35, P < 0.001) and shortened DT (180.0 ± 40.0 ms vs 190.0 ± 30.0 ms, P = 0.025). The peak A velocity and IVRT were increased in the NDHT group [(62.73 ± 13.82 ms vs 58.26 ± 12.40 ms, P = 0.002) and (90.0 ± 20.0 ms vs 80.0 ± 10.0 ms, P < 0.001), respectively]. Peak E velocity was similar in both groups. The prevalence of DD was increased in the NDHT group, 18.6% (32) vs 3.4% (6), P < 0.001. Of the 32 NDHT subjects who had DD, 84.4% (27) had no left ventricular hypertrophy (LVH) and 15.7% (5) had LVH. Diastolic function was negatively correlated with age, body mass index, systolic blood pressure, diastolic blood pressure and left ventricular mass index. Conclusion: Impairment in LVDF occurs in NDHT which may precede structural abnormalities. Hypertension, obesity, older age and LVH are associated with worsening of diastolic function.

Key words: Diastolic dysfunction, Diastolic heart failure, Left atrial size, Left ventricular hypertrophy, Left ventricular mass index

References

1 Department of Medicine
Universiti Kebangsaan Malaysia, Malaysia.
2 Cardiology Unit
Damansara Specialist Hospital, Malaysia
3 Faculty of Medicine
Universiti Teknologi MARA, Malaysia
Address for Correspondence: Dr Masliza Mahmod, Cardiology Unit, Department of Medicine, Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Bandar Tun Razak, 56000 Kuala Lumpur, Malaysia.
Email: dr_masliza@yahoo.com
Non-invasive assessment of diastolic function has been performed using 2-dimensional and Doppler echocardiography, colour Doppler M-mode, Doppler tissue imaging, radionuclide ventriculography and magnetic resonance-myocardial tagging. Invasive techniques such as cardiac catheterisation and simultaneous pressure and volume measurements represent the gold standard to assess LV diastolic function (LVDF); however, these are impractical for routine diagnostic evaluation.

In routine clinical setting, Doppler echocardiography provides the most useful information when compared to the others. The transmitral flow is assessed in the apical 4-chamber view with the pulsed Doppler sample volume at the tip of the mitral valves. Peak velocities of E (early passive atrial filling), A (late active atrial contraction), E/A ratio and deceleration time (DT) (representing time taken from rapid atrial filling to lose its velocity) are measured. Isovolumetric relaxation time can be measured by placing a continuous wave Doppler beam between the left ventricular outflow tract and the left ventricular inflow to measure the time from the aortic valve closure to mitral valve opening. All these parameters are influenced by heart rate, and both pre- and afterload.

Pulmonary venous flow can be assessed by transthoracic echocardiography by placing the sample volume in the right upper pulmonary vein from the apical 4-chamber view.

E/A ratio >1, DT between 150 and 220 ms and IVRT <100 ms are indicative of normal diastolic function. Diastolic dysfunction is considered when E/A ratio <1, DT >220 ms and IVRT >100 ms which is due to delayed relaxation of the left ventricle. Other forms of diastolic dysfunction that may mimic normal diastolic function are “pseudonormalisation” (E/A ratio >1, DT between 150 and 220 ms and IVRT between 60 and 100 ms) and “restrictive” pattern (E/A ratio >2, DT <150 ms and IVRT <60 ms). “Pseudonormalisation” can be caused by chronic hypertension and normal ageing process, whereas “restrictive” pattern which represents the most severe form of diastolic dysfunction can be caused by hypertrophic cardiomyopathy. This non-linear, “U-shaped” curve of E/A ratio makes it difficult to differentiate diastolic dysfunction versus pseudonormalisation from the E/A alone. The pulmonary venous flow pattern and tissue Doppler imaging provide further information to overcome these limitations.

Objective
To evaluate LV diastolic function in newly diagnosed hypertensives (NDHT) and to compare it with healthy volunteers.

Study Hypothesis
Our hypothesis was that impairment of diastolic function is present in NDHT.

Materials and Methods

Patient Selection
Inclusion criteria for the hypertensive group were aged between 30 and 50 years with an average systolic blood pressure (BP) ≥140 mm Hg and/or diastolic BP ≥90 mm Hg at enrolment, or who had been diagnosed to have hypertension for <6 months prior to enrolment. Controls were recruited from healthy volunteers, aged between 30 and 50 years, had normal BP at enrolment and were not known to have hypertension previously. Subjects were excluded if they had malignant or accelerated hypertension, significant valvular heart disease such as aortic stenosis, hypertrophic cardiomyopathy or ischaemic heart disease. All patients gave informed consent.

Study Design
This was a cross-sectional observational study conducted at Universiti Kebangsaan Malaysia, which was approved by the institution’s Research and Ethics Committee. There were 396 subjects recruited for this study consisting of 198 NDHT and another 198 healthy volunteers. Subjects were obtained by distributing pamphlets at Hospital Universiti Kebangsaan Malaysia, Family Medicine Clinics and government clinics in Hulu Langat, Selangor. Subjects who were willing to participate were invited to the Clinical Trial Wards. At enrolment, patients’ demographic data and medical history were obtained and recorded in a standardised Clinical Report Form. At the outpatient visit, heart rate was taken, and seated and standing BP were measured by using a mercury sphygmomanometer. The phase 1 Korotkoff sound was taken as systolic pressure and phase 5 as diastolic pressure. After resting for 10 minutes in a seated position, BP was determined by calculating the mean of 3 replicate measurements taken 1 minute apart. After 2 minutes of standing, 3 BP measurements were obtained. Body mass index (BMI) and waist-hip ratio (WHR) were calculated according to the standard formula. Body surface area (BSA) was calculated using the following formula:

$$\text{BSA} (m^2) = \sqrt{\frac{\text{Height(cm)} \times \text{Weight(kg)}}{3600}}$$

Echocardiography
Transoesophageal echocardiographic assessment by HP 5500 SONOS machine was done by a single trained ultrasonographer. The long axis parasternal, short axis and apical 4-chamber views were used. LVEF and left ventricular mass (LVM) were measured by standard echocardiographic criteria. Left ventricular mass was indexed for BSA to obtain LV mass index (LVMi). LVH was defined as LVMi >136 g/m² for men and >112 g/m² for women.
Indices of LVDF were derived from recordings of forward mitral flow by pulsed wave Doppler echocardiography from the apical 4-chamber view, providing beat-by-beat assessment of left ventricular filling. The peak early (E) diastolic forward mitral flow and late (A) diastolic velocities were measured. E/A ratio of <1 was taken as an indicative of diastolic dysfunction. DT, the interval from the peak of E velocity to its extrapolation to baseline and IVRT, time from aortic valve closure to mitral valve opening were also measured.

**Statistical Methods**

Data were analysed using the SPSS 11.0 statistical package. Quantitative and qualitative demographic characteristics were summarised and data were tabulated. Results were presented in tabulated and graphical format. Discrete variables were analysed by using the chi-square test and continuous variables were analysed by using the Student’s t-test. Associations between E/A ratio and other variables were examined using Pearson rank correlation. Values of $P < 0.05$ were considered as statistically significant. Data were expressed as mean ± standard deviation and proportion or percentage.

**Results**

**Demographic Data and Baseline Characteristics**

Between January and August 2004, 396 subjects were recruited. Of these, 198 were NDHT subjects and 198 normal controls. The baseline characteristics of both groups are shown in Table 1. The age and gender distributions were similar in both groups.

BMI and BSA were significantly higher in the NDHT group when compared to the control group. WHR was similar in both groups. There was no significant difference in the prevalence of diabetes mellitus in both groups. Smoking and alcohol consumption were more prevalent in the control group. The majority of subjects were Malays followed by Chinese and Indians (Fig. 1).

More subjects in the hypertensive group had a family history of hypertension and a large proportion of subjects had more than one family history of cardiovascular risk factors in both groups (Fig. 2).

**Echocardiography**

In this study, echocardiograms were performed in 347 subjects; 172 and 175 were performed in the NDHT and controls, respectively. The mean LVEF did not differ significantly in both groups. The mean left atrial (LA) size was slightly increased in the NDHT ($3.20 ± 0.45$ cm vs $3.12 ± 0.46$, $P > 0.05$). E/A ratio was reduced in the NDHT group ($1.27 ± 0.41$ vs $1.37 ± 0.35$, $P = 0.001$) (Table 2). The prevalence of diastolic dysfunction (E/A <1) was significantly increased in the hypertensive group; 32 (18.6%) vs 6 (3.4%), $P < 0.001$. There was an increase in peak-A velocity and IVRT with reduced DT. Peak-E velocity was similar in

![Fig. 1. Distribution of patients according to ethnic groups.](image-url)
Table 2. Echocardiographic Parameters in the Study Subjects

<table>
<thead>
<tr>
<th>NDHT (n = 172)</th>
<th>Control (n = 175)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak-E velocity (ms)</td>
<td>79.92 ± 15.83</td>
<td>76.96 ± 14.62</td>
</tr>
<tr>
<td>Peak-A velocity (ms)</td>
<td>62.73 ± 13.82</td>
<td>58.26 ± 12.40</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.27 ± 0.41</td>
<td>1.37 ± 0.35</td>
</tr>
<tr>
<td>E/A ratio &lt;1</td>
<td>32 (18.6%)</td>
<td>6 (3.4%)</td>
</tr>
<tr>
<td>DT (s)</td>
<td>0.18 ± 0.04</td>
<td>0.19 ± 0.03</td>
</tr>
<tr>
<td>IVRT (s)</td>
<td>0.09 ± 0.02</td>
<td>0.08 ± 0.01</td>
</tr>
<tr>
<td>Left atrium (LA) (cm)</td>
<td>3.20 ± 0.45</td>
<td>3.12 ± 0.46</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>64.2 ± 7.4</td>
<td>63.3 ± 7.1</td>
</tr>
</tbody>
</table>

A: late active atrial contraction; E: early passive atrial filling; DT: deceleration time; IVRT: isovolumetric relaxation time; LV: left ventricular; NDHT: newly diagnosed hypertensives; ns: not significant

Fig. 2. Family history of cardiovascular risk factors.

Fig. 3. Correlation between E/A ratio and various parameters.
both groups. Diastolic function was reduced with age, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP) and LVMI (Figs. 3a to 3e). However, it was not affected by WHR, BSA and LA size (r = -0.041, r = -0.061 and r = -0.011, P>0.05 respectively). Of the 32 subjects with diastolic dysfunction in the NDHT group, 27 (84.4%) had no LVH and only 5 (15.6%) had LVH. This suggests a compensatory physiological mechanism in response to pressure load during an early phase of hypertension before LVH is demonstrable. In contrast to a previous study, LV structural abnormalities were found to occur earlier than diastolic abnormalities in the early stage of hypertension.12

The peak-A velocity, which represents atrial contraction, was significantly increased in the NDHT without a significant increase in the LA size. In addition to that, there was no significant correlation between diastolic dysfunction and LA size. As previously thought, LA enlargement correlates with elevated mean pulmonary wedge pressure especially in chronic diastolic dysfunction.13 Thus, this compensatory physiological mechanism occurs very early before the presence of LA enlargement. There was a significant negative correlation between diastolic function and age, BMI, blood pressure and LVMI which has been well established previously.14,15

Limitations of Study

The use of E/A ratio for the measurement of diastolic function has some limitations. Ideally, measurements of pulmonary venous flow or tissue-Doppler imaging should be performed to identify patients with pseudonormalisation. However, the number is expected to be small and therefore would not significantly affect our observation.

Conclusion

Impairment in LVDF occurs in NDHT. Interestingly, the majority of patients with diastolic dysfunction had no LVH. This suggests that functional abnormality may occur prior to the occurrence of structural abnormality. Hypertension, obesity, older age and LVH are associated with worsening of diastolic function.

REFERENCES