Prevalence of Left Ventricular Diastolic Dysfunction among Hypertensive Adults in Klang Valley, Malaysia

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Abstract: Heart failure in many patients is due to left Ventricular Diastolic Dysfunction (LVDD), but little is known about its prevalence among hypertensive adults, especially in the primary care setting. , This quantitative study aims to evaluate the prevalence and factors associated with LVDD. A cross-sectional study was conducted among 359 hypertensive patients who underwent echocardiography to define their cardiac structure and function. The peak ratio of early to late diastolic filling velocity was used to assess the LVDD. The Framingham Coronary Heart Disease risk score was derived from the most recent blood test available in the previous year. SPSS version 19 was used to analyze the data. Echocardiographic LVDD was found in 68% of the participants. Of the 243 hypertensive subjects who had LVDD, 69.5% did not have any left ventricular hypertrophy (LVH) while 30.5% had LVH. Age (odds ratio (OR) 1.11, 95% confidence interval (CI) 1.07-1.15), fasting blood glucose (OR 1.18, 95% CI 1.02-1.37), poor blood pressure control (OR 1.93, 95% CI 1.12-3.32), central obesity (OR 2.06, 95% CI 1.17-3.64), and LVH (OR 2.76, 95% CI 1.29- 5.90) were found to have a significant positive relation with LVDD. Poor hypertension control, diabetes, older age, central obesity, and LVH are the predictors for the development of diastolic dysfunction.

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1. Introduction

Hypertension is one of the main causes of preserved Left Ventricular Ejection Fraction (LVEF) heart failure where diastolic dysfunction is present instead. Heart failure with normal left ventricular ejection fraction (HFNEF) or preserved LVEF heart failure also known as diastolic heart failure consists of a clinical syndrome characterized by the symptoms and signs of heart failure, a preserved ejection fraction (EF), and left ventricular diastolic dysfunction (LVDD) (1). The incidence of HFNEF is common in older females with diabetes and patients with uncontrolled blood pressure (2, 3, and 4). As such, it could become the most common type of heart failure in the community as the aging population increases substantially worldwide (5-8). In addition, studies have reported that the prognosis of HFNEF is ominous and comparable to heart failure with reduced ejection fraction (9-12). However, the importance of this public health problem has been under-recognised as it is undiagnosed in most of the patients, resulting in a lack of optimal treatment in the community.

Early diagnosis of LVDD is essential as studies have shown that pre-clinical LVDD is the first observable manifestation of heart failure (5, 13). LVDD has also been found to be associated with marked increases in all-cause mortality and morbidity in many studies (8, 14, and 15). However, little is known about the characteristics that predispose individuals to anabnormal diastolic function among hypertensive individuals in the primary care setting. Such information is essential for improving adherence to clinical practice guidelines since treatment at an early asymptomatic stage may delay or prevent progression to symptomatic heart failure and its consequences. Thus, this study aims to determine the prevalence and predictors of diastolic dysfunction among hypertensive individuals in the primary care setting.

2. Material and Methods

This cross-sectional study was conducted in a hospital-based outpatient clinic in Klang Valley, Malaysia. The inclusion criteria were patients with hypertension, as determined when their case record fulfilled the following criteria:

- Either documented diagnosis of hypertension according to World Health

Organization (WHO)-International Hypertension Society (ISH) criteria, or:

- Those whose current treatment consisted of lifestyle modification or anti-hypertensive agents.

Patients with hypertension who were 18 to 70 years old were recruited from 1st of June 2009 to 30th of September 2009. We choose an arbitrary upper age limit of 70 years in this study in order to avoid the widely known effect of aging on the mitral inflow patterns on echocardiogram (3).

Demographic data and smoking status of the patients were obtained during face-to-face interviews. Co-morbidities, including diabetes, ischaemic heart disease (IHD), and stroke, were also recorded. Lipid profile and fasting blood glucose were obtained from patient records in 2009. The Framingham CVD risk scores (FRS) were calculated based on age, total and high-density lipoprotein cholesterol, systolic blood pressure, treatment for hypertension, smoking, and diabetes mellitus status.

All patients underwent echocardiography tests to clarify the cardiac structure and function. Classical M-mode with a two-dimensional Doppler echocardiography video recorder was used, together with a Siemens model equipped with 2.5 MHz transducer. Subjects were examined in the left lateral decubitus position with left parasternal, and the apical chamber views were taken as indicated during the test(16).The peak early (E) and late (A) diastolic velocities were measured from the transmitral flow signal. LVDD was diagnosed by looking at the E/A ratio reading; "E wave velocity" stands for the highest velocity during the early rapid filling diastolic phase and "A wave velocity" refers to the highest velocity during the late filling (atrial systole) phase. The E/A ratio is derived from the ratio of the peak early ventricular filling velocity to the peak atrial filling velocity. In a normal situation, the E/A ratio falls between 1 and 2; in LVDD, the E/A ratio is < 0.75 (17), in which there is a decrease in early transmitral LV filling and an increased proportion of filling during atrial contraction. HFNEF was diagnosed when the patient had clinical symptoms suggestive of heart failure, together with the presence of LVDD in a preserved ejection fraction. Echocardiography left ventricular hypertrophy (LVH) is defined as the left ventricular posterior wall thickness together with the inter-ventricular septal thickness ⩾11mm (18).

Patients' height and weight were determined using a digital scale. Body mass index (BMI) was calculated as weight in kilograms per square of the height in meter (kg/m^2). Abdominal obesity was obtained using a measuring tape according to standard procedure. Using the Asian Pacific's obesity guideline, obesity and central obesity were defined as having a BMI of more than 27.5 kg/m^2 and waist circumference ≥ 90cm in men and ≥ 80 cm in woman respectively (19). Blood pressure was taken using a mercury sphygmomanometer. The average of three blood-pressure readings was used to determine the control of blood pressure. The target blood pressure (BP) was defined as <140/90 mmHg among hypertensive patients and <130/80 mmHg among hypertensive patients with diabetes (20, 21). SPSS statistical software version 19 (SPSS IBM New York, United States) was used. Continuous data are described as mean and standard deviation or median and interquartile range (25-75th percentiles) if the distribution is skewed. Categorical data are reported as proportions (percentage). The Chi-square test was used to examine the associations among the different variables of the study. Multivariate logistic analysis was used to look for the predictors of the diastolic dysfunction. All analyses were done with 95% confidence intervals (CI), and the level of significance was determined at $p<0.05$. Ethical approval was obtained from the Medical Ethics Committee of the Faculty of Medicine University Malaya.

3. Results

A total of 359 patients with hypertension were enrolled in the study. However only 356 respondents were enrolled in the analyses as three of the echocardiography results were not reliable for LVDD diagnosis. The median age of patients was 59.4 ±10 years, with 52.1% being aged >60 years. The median duration of BP was 8 ± 12 years, and patients' mean systolic blood pressure was136.3 ± 13.9 mmHg while mean diastolic blood pressure was 81.5 ± 7.7 mmHg. The mean BMI was 26.8 ± 4.7 kg/m2.

Table 1. The demographic and clinical Characteristics of the study populations (n= 356)

Variables	Value
Age, years	59.4 ± 10
Females, n (%)	208 (58%)
Race, Malay: Chinese: Indian, n (%)	99,180,76 (27.6%,50.1%,21.2)
Co-morbidities, n (%)	44 (12.3%)
Diabetics' hypertensive, n (%)	147 (40.9)
Duration of blood pressure (years)	8 ± 12 years
Mean blood pressure (mmHg)	136.3 ± 13.9/ 81.5 ± 7.7
ACEI/ARB use, n (%)	203 (56.5)
Statin use, n (%)	258 (71.9)

Participants were predominantly female (58%), Chinese (50.1%) and individuals who had completed secondary education and above (86.1%). Females were found to have a better blood pressure control rate than males (41.5% versus 40.9%) and a lower percentage of LVH (19.5% versus 29.5%).Vascular co-morbidities were recorded among 44 (12.3%) individuals. Stroke was more common than cardiovascular events (7.5% versus 6.7%). The majority of patients were treated with ACEI or ARBs (56.5%). Demographic and clinical characteristics of all patients who met the study inclusion criteria are shown in Table 1.

Table 2. Patients' Clinical Characteristics Based on LV Diastolic Function

Characteristics	**Overall (n=356)**	**Presence of LVDD (n=243)**	**Absence of LVDD (n=113)**	**P-value**
Age, years	59.3 ± 7.5	60.7 ± 6.4	56.5 ± 8.7	<0.001
Target BP achieved (n, %)	147 (41.3)	153 (63.0)	56 (49.6)	0.017
Left ventricular hypertrophy (n, %)	85 (23.9)	74 (30.5)	11 (9.7)	0.001
Central obesity (n, %)	213 (59.8)	157 (64.6)	56 (49.3)	0.007
Fasting plasma glucose (n, %)	6.6 ± 2.1	6.8 ± 2.4	6.0 ± 1.4	0.006
Female gender (n, %)	207 (58.1)	138 (56.8)	69 (61.1)	0.447
Ischaemic heart disease (n, %)	22 (6.2)	19 (7.8)	3 (2.7)	0.073
Framingham risk score points (n, %)	20.7(8.2)	22.6 (7.7)	16.7(7.6)	0.001
Duration of BP, months	125 ± 88	133 ± 90	107 ± 82	0.148
Smoking (n, %)	25(7.0)	14(5.8)	11(9.7)	0.919
Consume alcohol (n, %)	98 (27.5)	65(26.7)	33(29.2)	0.629
ARB/ ACEI agents	200(56.2)	141(58.0)	59(52.2)	0.304
BMI ± SD, kg/m2	26.8 ± 4.7	27.1 ± 4.6	26.1 ± 4.9	0.064
Home BP monitoring (n, %)	177(49.7)	126(51.9)	51(46.4)	0.090

ARB: Angiotensin Receptor Blockers
ACEI: Angiotensin Converting Enzyme Inhibitors
BP: Blood pressure
*statistically is significant as the p-value is <0.005

Table 3. Factors associated with left ventricular diastolic dysfunction

Characteristics	**Univariate model**		**Multivariate model**	
	OR (95% CI)	P Value	OR* (95% CI**)	P Value***
Age	1.08(1.05-1.11)	<0.001	1.11(1.07-1.15)	<0.001
Poor BP control	1.73(1.10-2.72)	0.017	1.93(1.12-3.32)	0.018
Left ventricular hypertrophy	4.06(2.06-8.01)	<0.001	2.76(1.29-5.90)	0.009
Central obesity	1.86(1.18-2.92)	0.007	2.06(1.17-3.64)	0.012
Fasting plasma glucose	1.22(1.06-1.40)	0.006	1.18(1.02-1.37)	0.025
Female gender	1.19(0.76-1.88)	0.447	0.85(0.49-1.49)	0.574
Ischaemic heart disease	0.32(0.09-1.11)	0.073	1.76(0.46-6.82)	0.411
Framingham risk score points	1.09(1.06-1.12)	<0.001	1.02(0.97-1.06)	0.461

* OR: Odds Ratio
** CI: Confidence Interval
***statistically is significant as the p-value is <0.005
* Adjusted for age, blood pressure control left ventricular hypertrophy, central obesity, fasting blood sugar, female gender, ischemic heart disease and Framingham risk scores.

The prevalence of echocardiography LVDD and HFNED was 68% and 10.3%, respectively. Of the 243 hypertensive subjects who had LVDD, 30.5% had LVH. Subjects with LVDD were found to be older and have poorer blood pressure control, left ventricular hypertrophy, central obesity, fasting plasma glucose, and higher Framingham risk scores. The clinical characteristics and the left ventricular diastolic dysfunction statuses on the echocardiogram of all patients are shown in Table 2.

Table 3 shows the odds of having LVDD based on multiple logistic regressions after adjusting for established LVDD risk factors. Patients who are older (odds ratio (OR) 1.11, 95% confidence interval (CI) 1.07, 1.15) with poorer blood pressure control (OR 1.93, 95% CI 1.12, 3.32), higher fasting plasma glucose (OR 1.18, 95% CI 1.02, 1.37), central obesity (OR 2.06, 95%CI 1.17, 3.64), and underlying LVH (OR 2.76, 95% CI 1.29, 5.90) were significantly associated with the development of LVDD. However, no correlation existed between both mean FRS and LVDD.

4. Discussions

In our study, the overall prevalence of LVDD among hypertensive patients, as estimated from echocardiography measurement, was as high as 68%. The prevalence of diastolic heart failure was 10.3%. The reported prevalence of LVDD in hypertensive patients varies from 46% to 85% (22-26). The prevalence is varies widely as the characteristics of the studied population, choice of imaging modalities, and criteria used to diagnose LVDD varied in the previous studies. This result is in keeping with other studies in Europe and Africa. Although the majority of patients with the LVDD in this study were asymptomatic, we still need to be vigilant as study reported that nearly a fifth of diastolic dysfunction was associated with the subsequent development of heart failure (27) in which suggesting a high progression of LVDD to overt heart failure. Besides that, hypertension (HPT) is currently one of the most common public health problems in Malaysia (28) as the lifespan has increased in the population (29, 30). With the lifespan expected to continue to increase, the prevalence of hypertension is also expected to increase (20). Hypertension is often associated with increased risk of cardiovascular disease, which subsequently leads to the development of heart failure. These results should also prompt us to use more ACEI/ARB, if not already used, as these agents have been shown to slow down the progression to diastolic heart failure (31, 32). Furthermore, doctors need to adhere more to the national practice guidelines and provide optimal treatment of BP to delay the new onset of diastolic heart failure.

Our study found that age is one of the factors associated with the development of LVDD, which concurs with many other studies (2, 3, and 33). This can be explained by the fact that hypertension actually amplifies the vascular changes in the aging heart and worsens the decrease in left ventricular compliance, resulting in physical deconditioning (34). Our study indicated that LVH is a predictor of the presence of LVDD. One possible explanation of why LVH causes LVDD could be because of the enhanced sensitivity to volume overload from the increase in left ventricular remodeling and dilatation of with volume-dependent elevation of the filling pressures (4). Similarly, uncontrolled chronic hypertension seems to be the main culprit of LVH, which subsequently causes the development of LVDD and heart failure (35, 36, and 37).

Surprisingly, central obesity was shown to have a relationship with the LVDD instead of BMI as reported by other studies (38). Asians are known to have higher abdominal obesity despite having the same BMI (36). In other words, central obesity is more accurate and better at representing the CV risk factors, particularly in the Asian population (37). Furthermore, insulin resistance has been reported to be an independent predictor for LVDD (35, 39), which explains this finding.

With regard to other factors, in our study, we observed that LVDD was strongly predicted by the diabetic hypertensive disorder. According to the literature, glucose intolerance and type two diabetes mellitus negatively impact the midwall systolic mechanism and diastolic filling, as mentioned in the Strong Heart Study and HyperGEN study (40, 41, and 42). Thus, this may explain LVDD is the early manifestations of diabetic cardiomyopathy (43). In addition, the prevalence of T2DM is reported to be much higher in hypertensive patients than the common population (44, 45) Thus, not surprisingly the risk of death from the cardiovascular event is absolutely higher among hypertensive patients with underlying diabetes, as shown in the literature (46).

Previous studies have shown that Framingham risk score has a relationship with left atrial volume, which is a surrogate in expressing the severity of diastolic dysfunction (47). However, our study failed to show such a relationship between Framingham risk score and LVDD. This is probably because the FRS may underestimate the CVD risk in those high-risk groups such as Asian population and diabetes patients (48, 49, and 50). Indeed, 40.9% of the patients in our study had underlying diabetes,

which may explain the negative association between LVDD and FRS in our study.

In terms of gender, females were found to have a better blood pressure control rate than males (41.5% versus 40.9%) and a lower percentage of LVH (19.5% versus 29.5%). This could explain the negative relationship between female gender and the development of LVDD; however, further study is needed to examine this aspect.

Cardiac catheterization remains the gold standard for diagnosing diastolic dysfunction. However, the use is restricted as this is an invasive procedure and not practical in routine daily practice. Tissue Doppler imaging sounds to be a better tool compared to the conventional standard echocardiography given that its measurement of the transmittal flow is independent of other confounding factors. However, this tool is not available in the primary care setting.

In summary, the prevalence of LVDD is high among the hypertensive population in the primary care setting. Every effort needs to be put in for early detection. Older age, poorer blood pressure control, presence of left ventricular hypertrophy, central obesity, and fasting plasma glucose levels were significantly associated with a higher risk of LVDD.

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