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Correlation between Hypertension and Left Ventricular Diastolic Dysfunction in the Elderly: A Cross-Sectional Study in China

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Abstract

Background: Hypertension is recognized as a risk factor for the development of left ventricular hypertrophy (LVH) and left ventricular diastolic dysfunction (LVDD). These cardiac abnormalities collectively form hypertensive heart disease and can eventually progress to heart failure (HF). LVDD has been linked to a higher risk of cardiovascular mortality. Consequently, addressing and improving LVDD is a crucial therapeutic goal in patients with hypertension. To investigate the prevalence of hypertension and LVDD, this cross-sectional survey was conducted among the elderly population residing in Jinshan District, Shanghai, China.

Methods: A total of 2584 subjects who at least aged 65 years old, representing the general population of the cohort, participated in this study. They underwent a series of evaluations, including physical examination, questionnaire survey, serological testing, and comprehensive echocardiography examination, which were conducted as part of routine clinical practice. Based on their hypertension history and blood pressure measurements, participants were categorized into two groups: hypertension group and normotension group. Among them, 902 cases (72.1% of whom were female) were diagnosed with LVDD.

Results: In the comparison between participants with hypertension and LVDD and those without LVDD, it was found that the former group had higher age, a higher proportion of females, increased heart rate (HR), and elevated N-terminal pro-B natriuretic peptide (NT-pro BNP) level. Furthermore, patients with hypertension and LVDD were less likely to have obesity, diabetes mellitus (DM), coronary artery disease (CAD), dyslipidemia,

and smoking habits. Similarly, when comparing participants with normotension and LVDD to those without LVDD, older age, a higher proportion of females, the increased body mass index (BMI), and the elevated NT-pro BNP level in the normotension group were noted. Additionally, patients with normotension and LVDD were more likely to have obesity, DM, CAD, and smoking habits, while less likely to have dyslipidemia. Regarding left ventricular (LV) geometry, it was revealed that 203 (22.5%) participants exhibited LV concentric remodeling, 432 (47.8%) participants exhibited concentric LVH, and 107 (11.8%) participants exhibited eccentric LVH among those with LVDD. The prevalence of different LV geometries did not significantly differ between the hypertension and normotension groups. Furthermore, multivariate logistic regression analysis demonstrated that LVH was associated with LVDD, female gender, and aging.

Conclusion: In the normotension group with LVDD, a higher prevalence of obesity, DM, CAD, and smoking habits was observed. There were no significant differences in the prevalence of LV concentric remodeling, concentric LVH, and eccentric LVH between the hypertension and normotension groups. Additionally, female gender and aging were found as independent factors associated with LVH in LVDD among the elderly population.

Keywords: Left ventricular diastolic dysfunction; Hypertension; Left ventricular geometry; Elderly

Introduction

Heart Failure (HF) and Left Ventricular Diastolic Dysfunction (LVDD) are the most common cardiac complications of Hypertension (HTN), particularly in elderly [1,2]. Anatomical and functional changes, such as Left Ventricular Hypertrophy (LVH) and left atrial enlargement, are commonly observed in the cardiac system of individuals with long-term HTN. The sustained pressure overload can lead to the progression of Left Ventricular Diastolic Dysfunction (LVDD) and eventually result in HF [3]. Asymptomatic or symptomatic LVDD can be attributed to several major risk factors, including HTN, LVH, aging, obesity, and Diabetes Mellitus (DM). Recent studies have shed light on the association between these risk factors and the development of LVDD [4-6]. Evaluation of cardiac target organ damage in patients with long-term HTN has traditionally involved routine assessment of cardiac structure and diastolic function. These assessments serve as crucial methods to gauge the impact of HTN on the heart and its associated complications. However, it is worth noting that several studies have included elderly individuals with various cardiovascular comorbidities, including HTN, obesity, metabolic syndrome, and DM. These comorbidities can contribute to different patterns of Left Ventricular (LV) geometric remodeling. Traditionally, LV geometry has been categorized into four patterns: normal geometry, concentric remodeling, eccentric hypertrophy, and concentric hypertrophy. As HTN and LV diastolic dysfunction progress, the concentric hypertrophy pattern becomes more prevalent and is associated with a higher risk of cardiovascular events. Therefore, in our survey, we aimed to assess the distribution of LV geometries with LV diastolic dysfunction between individuals with HTN and those with normal tension in the elderly population. The aim of this study was to investigate the impact of LVDD and LV geometries in individuals with and without HTN, and to analyze the correlation with cardiovascular comorbidities, including obesity, DM, dyslipidemia, and Coronary Artery Disease (CAD).

Methods

Inclusion and exclusion criteria

Subjects who at least aged 65 years old were recruited from the Shanghai Heart Health Study (SHHS, China) in 2014 [7]. This cohort study aimed to investigate the incidence, prevalence, morbidity, and mortality of cardiovascular diseases in the Jinshan District community of Shanghai. During the 2014 follow-up period, a total of 3305 subjects completed echocardiography and were enrolled in the study [8]. After excluding subjects with incomplete data, a total of 2584 subjects were included in the analysis. All participants provided basic information through self-completed questionnaires, underwent physical examination, had their serum biochemical parameters assessed, and underwent standard 12-lead Electrocardiogram (ECG) and echocardiography. This study adhered to the ethical guidelines outlined in the 1975 Declaration of Helsinki and received approval from the Ethics Committee of Zhongshan Hospital, Fudan University. Informed consent was obtained from each participant during the recruitment period. Subjects with incomplete biochemical or echocardiographic data were excluded from the analysis. Additional exclusion criteria were applied, including: (1) Left Ventricular Ejection Fraction (LVEF) ≤ 40%, (2) Left Ventricular End-Diastolic Volume Index (LVEDVI) > 97 ml/m^2, (3) presence of atrial fibrillation, (4) poor ultrasound imaging quality, significant valvular disease, prior valve replacement, and presence of tachycardia without identifiable mitral flow pattern.

Echocardiographic assessment

Transthoracic echocardiography was performed by an experienced sonographer using a 2.5 or 3.5 MHz probe (Philip IE33, Germany) following standardized protocols. Measurements were obtained in real-time and digitally recorded, with each participant assigned a unique identification consisting of their initials and study number. Echocardiograms were interpreted by cardiologists who were blinded to the participants' clinical data. Two-dimensional and Doppler images were acquired from parasternal long and short axes, as well as from apical 4-chamber and 2-chamber views. M-mode echocardiography was performed from the parasternal long-axis view. All recordings included a minimum of 3 heart cycles and were stored digitally for subsequent offline analysis. Left Ventricular End-Diastolic Diameter (LVEDD), Left Ventricular End-Systolic Diameter (LVESD), Left Ventricular Septal Thickness (IVST), and Posterior Wall Thickness (PWT) were measured using M-mode or two-dimensional echocardiography at the parasternal long-axis position. The Relative Wall Thickness (RWT) was calculated as the ratio of PWT plus IVST thickness to LVEDD. According to Devereux et al. [9] research, Left Ventricular Mass Index (LVMI) was calculated as $0.8 \times 1.04[(LVEDD + IVST + PWT)^3 + LVEDD^3] + 0.6$, divided by Body Surface Area (BSA). LVEF was determined by measuring Left Ventricular End-Systolic Volume (LVESV) and LVEDV using the apical 4- and 2-chamber views, employing an improved biplanar Simpson method. Left atrial volume was measured in a similar manner, and Left Atrial Volume Index (LAVI) was calculated using BSA. Pulse wave Doppler echocardiography recorded the apex of the mitral valve on the four-chamber section of the apical view using a sample volume. Early (MV-E) and late (MV-A) peak diastolic velocities, E/A ratio, and Deceleration Time (DT) were used as indicators of left ventricular end-diastolic pressure. Pulsed-wave Tissue Doppler Imaging (TDI) of the lateral wall under the apical four-chamber view evaluated the peak mitral annular velocity in early (E') and late (A') diastolic periods.

Clinical, demographic, and biochemical parameters

Clinical and demographic data, such as age, sex, smoking status, and pre-existing medical conditions, were collected from all subjects using questionnaires. Additionally, the subjects' height and weight were recorded.

Waist circumference was measured using a flexible, non-expandable tape between the lower thoracic cavity and the iliac crest while the subject was in a standing position. Blood pressure was measured and documented with a manual mercury sphygmomanometer after the subjects had sat and rested for 5 minutes. Following a 5-minute period in the supine position, the Heart Rate (HR) was determined using a standard 12-lead electrocardiogram. Any history or presence of atrial fibrillation, including paroxysmal and persistent atrial fibrillation, was noted from the ECG records.

HTN was diagnosed based on a continuous resting blood pressure measurement greater than 140/90 mmHg or a confirmed medical history of HTN. Coronary Heart Disease (CHD) was defined as a history of myocardial infarction or angina, or the presence of coronary artery stenosis greater than 70% confirmed by angiography. Patients with a documented history of diabetes, use of oral hypoglycemic agents or insulin, or Fasting Blood Glucose (FBG) levels equal to or exceeding 7 mmol/L were classified as having diabetes. Body Mass Index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters **[2].** Obesity was defined as BMI equal to or greater than 28 kg/m^2, or a waist circumference of 85 cm or more for men, and 80 cm or more for women. Patients with a confirmed medical history or meeting any of the following criteria were classified as having dyslipidemia: Total Cholesterol (TC) equal to or greater than 6.22 mmol/L, triglycerides equal to or greater than 2.26 mmol/L, Low-Density Lipoprotein Cholesterol (LDL-C) equal to or greater than 4.14 mmol/L, or High-Density Lipoprotein Cholesterol (HDL-C) less than 1.04 mmol/L. Individuals who smoked more than three cigarettes per day for at least one year were classified as smokers, including both former and current smokers.

Laboratory examinations

Venous blood samples from the subjects will be collected following a 12-hour fasting period. The collected blood samples will be transferred to the Central Laboratory of Zhongshan Hospital daily. After centrifugation and routine blood tests, the serum will be stored at -28 ℃ until further analysis. All procedures will be conducted using standard techniques. The N-terminal pro-B Natriuretic Peptide (NT-pro BNP) level was measured using a fully automatic electrochemical luminescence immunoassay on the Elecsys 1010 system (Roche Diagnostics, Basel, Switzerland).

Diagnostic criteria for LVDD and LVH

The diagnosis of LVDD is performed using conventional and TDI echocardiographic techniques, which are in accordance with the guidelines provided by the European Society of Cardiology (ESC) for Heart Failure and Echocardiography[10]. In this study, LVDD was diagnosed based on the criteria proposed by the ESC and Euy-Myoung Jeong, with minor modifications [10,11]. The presence of LVDD was determined if any of the following criteria were met: (1) E/E' ratio ≥8, (2) E/A ratio <0.5 and DT >280 ms, (3) LVMI >149 g/m^2 (male) or LVMI >122 g/m^2 (female), or (4) left atrial volume index (LAVI) >34 ml/m^2. Left ventricular geometric anomalies were categorized as follows: (1) LV concentric remodeling (normal LVMI combined with RWT ≥0.43), (2) eccentric LVH (increased LVMI combined with RWT <0.43), and (3) concentric LVH (increased LVMI combined with RWT ≥0.43).

Statistical analysis

LVDD patients were stratified into two groups: the HTN group and the normal blood pressure group based on their history of HTN and blood pressure during physical examination. Continuous variables were analyzed using t-tests or Wilcoxon rank sum tests, while categorical variables were analyzed using chi-square tests. Single

logistic regression analysis and multiple logistic regression analysis were conducted to assess the correlation between variables. Explanatory variables were selected based on their univariate correlation with the dependent variables. The multivariate regression model included variables that exhibited a significant correlation with the dependent variables of interest in the univariate analysis ($P < 0.01$). The statistical analysis was performed using Stata 12.0 software (College Station, TX, USA). A P-value less than 0.05 was considered statistically significant.

Results

Participants' characteristics

Participants were divided into two groups: the HTN group and the normotension group, with 1270 (53.9%) participants in the HTN group. Among all participants, 902 (38.3%) were diagnosed with LVDD, of whom 541 (60%) had HTN and 361 (40%) had normotension. The mean age of participants was 76.2±5 years old, and 72.0% of them were female. Among those with LVDD, 924 (39.2%) were diagnosed with LVH, and 432 (47.9%) had LVDD. In Table 1, it can be observed that the HTN subjects with LVDD were older, had a higher proportion of females, a higher HR, and a similar BMI compared with the non-LVDD group. The comorbidities of DM, dyslipidemia, obesity, CHD, and smoking were similar between the HTN subjects with LVDD and those without LVDD. Additionally, the mean NT-pro BNP level was higher in the HTN group with LVDD.

Table 1: Characteristics of LVDD participants with hypertension and normotension.

	Total	LVDD	non-LVDD	*P*
Hypertension (n=1270)				
Age (yrs)	76±5.9	76±5	74±6	< 0.001
Female (N %)	57.8	72	47.2	< 0.001
HR (bpm)	72±9	73±10	72±9	< 0.01
BMI (kg/m^2)	24.2±3.7	24.7±3.5	23.4±3.1	0.356
DM (N %)	11.6	87.7	13.9	0.134
CHD (N %)	2.8	77.8	22.2	0.734
Dyslipidemia (N %)	45.4	84.2	15.8	0.256

Obesity (N %)	30.4	80.1	20.5	0.634
Smoke (N %)	7.8	81.2	18.8	0.185
NT-pro BNP (pg/ml)	113.5 (59.4, 198.9)	79.5 (59.4, 197.7)	163.8 (44.9, 122.8)	< 0.001
Normotension (n=1084)				
Age (yrs)	75±5	75±5	74±5	0.257
Female (N %)	57.2	72.3	59.7	0.095
HR (bpm)	71±9	71±8	71±9	0.618
BMI (kg/m^2)	23.1±3	24.4±3	23.1±3	< 0.001
DM (N %)	8.1	12.2	6.1	< 0.001
CHD (N %)	2.3	3.6	1.7	< 0.05
Dyslipidemia (N %)	55.1	52.6	56.3	0.253
Obesity (N %)	9.5	13.2	7.6	< 0.01
Smoke (N %)	14.4	9.1	17.1	< 0.001
NT-pro BNP (pg/ml)	106.7 (55.7, 175.6)	129.5 (56.7, 187.7)	93.2 (45.7, 105.8)	< 0.001

Abbreviations: HR: heart rate; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; DM: diabetes mellitus; CHD: coronary heart disease; NT-pro BNP: N-terminal pro-B type natriuretic peptide. Values of NT-pro BNP are median (interquartile), other values are mean ±SD or %. Subjects compared with and without HTN group.

Furthermore, it was found that subjects with normotension and LVDD were no differences in gender and age, and BMI and HR were similar compared with the non-LVDD group. These normotension subjects with LVDD had a higher prevalence of comorbidities, such as DM, obesity, CHD, and smoking, and similar prevalence of

dyslipidemia compared with the non-LVDD group. The mean NT-pro BNP level was higher in the normotension with LVDD group.

Echocardiographic indices of participants

Table 2 displayed that HTN subjects with LVDD had higher values of MV-E, MV-A, DT, IVST, PWT, LVEDVI, E/A, E/E', LAVI, LVMI, and lower values of E' compared to the non-LVDD group. The LVEF was similar between the LVDD and non-LVDD groups. Similarly, normotension subjects with LVDD exhibited higher values of MV-E, MV-A, IVST, PWT, LVEDVI, E/A, E/E', LAVI, LVMI, and lower values of E' compared with the normotension group. DT and LVEF were similar between the LVDD and without LVDD groups.

Table 2: Echocardiographic data of LVDD participants with hypertension and normotension.

	Total	LVDD	non-LVDD	*P*
Hypertension (n=1270)				
MV-E (cm/s)	73.1±15	72.2±15	59.4±14	< 0.001
MV-A (cm/s)	92.0±17	93.7±17	84.9±17	< 0.001
DT (ms)	207.5±52	207.8±52	195.7±51	< 0.001
IVST (cm)	9.5±1.2	9.6±1.3	9.3±1.2	< 0.01
PWT (cm)	9.3±1.1	9.3±1.1	9.2±1.1	< 0.01
LVEDVI (ml/m^2)	46.7±8	45.2±8	42.9±8	< 0.001
LVEF (%)	66.5±4	66.7±4	66.1±3	0.767
E ' (cm/s)	7.0±1.5	6.9±1.4	8.3±1.5	< 0.01
E/A	0.8±0.2	0.8±0.2	0.7±0.3	< 0.001
E/E '	10±2	10±1	6±1	< 0.001
LAVI (ml/m^2)	34.8±9	35.9±9	29.4±8	< 0.001

LVMI (g/m^2)	101.5±23	100.9±24	96.2±22	< 0.01
LVH (%)	38.5	48.1	31.4	< 0.001
Normotension (n=1084)				
MV-E(cm/s)	64.5±15	73.2±16	60.1±12	< 0.001
MV-A(cm/s)	83.8±16	91.2±17	79.8±14	< 0.001
DT (ms)	206.8±50	206.7±53	206.6±49	0.847
IVST (cm)	9.2±1.1	9.3±1.2	9.1±1.1	< 0.05
PWT (cm)	9.1±1.0	9.2±1.0	8.9±1.0	< 0.001
LVEDVI (ml/m^2)	45.8±7.2	46.2±8.1	44.1±7.0	< 0.001
LVEF (%)	61±6	60±6	61±6	0.805
E＇(cm/s)	8.5±2.1	7.1±1.5	9.2±2.0	< 0.001
E/A	0.7±0.2	0.8±0.3	0.7±0.2	< 0.001
E/E＇	8.0±2.1	10.6±2.5	6.7±1.5	< 0.001
LAVI (ml/m^2)	30.5±7	33.4±8	29.2±6	< 0.001
LVMI (g/m^2)	99.8±22	101.2±23	97.4±21	< 0.01
LVH (%)	40.1	47.7	36.4	< 0.001

Abbreviations: MV-E: Early Diastolic Transmittal Flow Velocity; MV-A: Late Diastolic Transmittal Flow Velocity; DT: Declaration Time; IVST: Interventricular Septal Thickness; PWT: Posterior Wall Thickness; LVEDVI: Left Ventricular End Diastolic Volume Index; LVEF: Left Ventricular Ejection Fraction; E′: Early Diastolic Mitral Annular Velocity; LAVI: Left Atrial Volume Index; LVMI: Left Ventricular Mass Index. Values

are mean ±SD or %. Subjects compared with and without HTN group.

Distribution of LV geometries

Table 3 demonstrated that there was no significant difference in the distribution of normal LV geometry, concentric LV remodeling, eccentric LVH, and concentric LVH between the HTN and normotension groups with LVDD ($P > 0.05$). **Figure 1** displayed that the number of individuals with normal LV geometry and eccentric LVH was higher across all three age groups. **Figure 2** revealed that the number of individuals with different LV geometries in LVDD patients was higher in females compared to males. **Figure 2** indicated that the number of individuals with different LV geometries in LVDD patients with HTN was also higher in females compared to males.

Table 3: Distribution of LV geometries with hypertension and normotension.

	LVDD (n=902)	HTN (n=541)	Normotension (n=361)	*P*
Normal LV geometry (%)	41.5	41	42.1	0.749
Concentric LV remolding (%)	10.6	10.9	10.2	0.754
Eccentric LVH (%)	36.2	35.3	37.1	0.578
Concentric LVH (%)	11.9	12.8	10.5	0.311

Abbreviations: LV: Left Ventricular; LVH: Left Ventricular Hypertrophy. Values are %. Subjects compared with and without HTN group used Chi-square test.

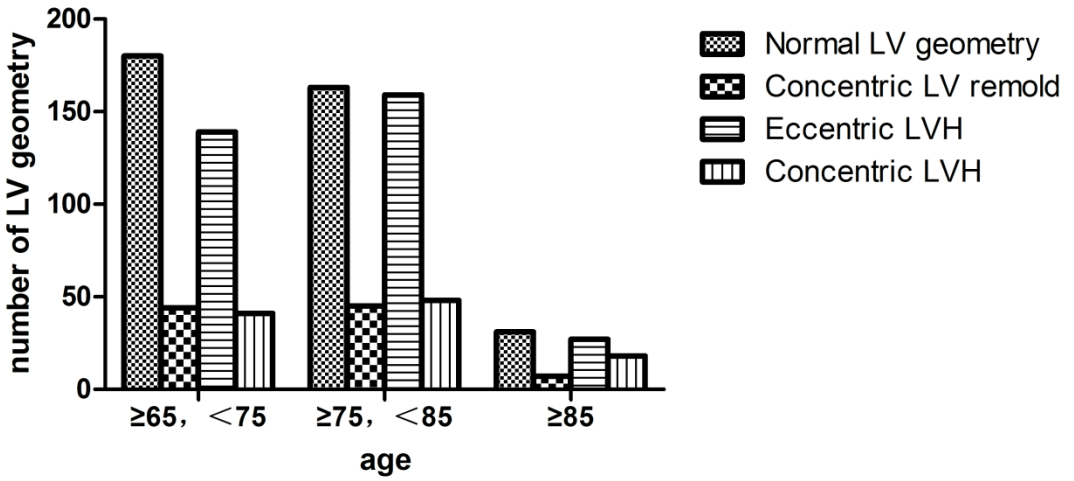

Figure 1: Number of LV geometry in age group.

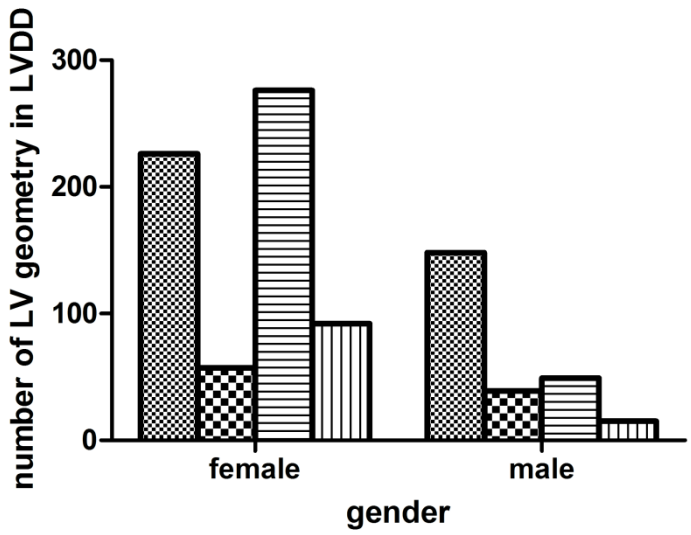

Figure 2: Number of LV geometry in different gender.

Factors influencing LVDD and LVH subjects

Table 4 presents the results of multivariate logistic regression analysis, indicating that LVDD was significantly associated with female gender, older age, LVH, CHD, HTN, DM, and obesity. In **Table 5,** the multivariate logistic regression analysis revealed that LVH was significantly associated with female gender and older age.

Table 4: Multiple Logistic regression of LVDD subjects.

LVDD	Multiple regression		
	OR	95% CI	*P*
Female	2.686	2.163-3.335	＜0.001
Age	1.076	1.059-1.093	＜0.001
LVH	1.351	1.122-1.688	＜0.001
CHD	1.806	1.068-3.006	＜0.05
HNT	1.401	1.168-1.678	＜0.001
DM	1.523	1.176-1.973	＜0.01
Smoke	0.961	0.713-1.295	0.797
Obesity	1.315	1.095-1.579	＜0.01

Abbreviations: LVDD: Left Ventricular Diastolic Function; LVH: Left Ventricular Hypertrophy; HNT: Hypertension; DM: Diabetes Mellitus.

Table 5: Multiple Logistic regression of LVH subjects.

LVH	Multiple regression		
	OR	95% CI	*P*
LVDD	1.341	1.113-1.614	＜0.01
Female	4.017	3.194-5.052	＜0.001
Age	1.026	1.011-1.043	＜0.001
Smoke	1.249	0.913-1.708	0.163

Abbreviations: LVH: Left Ventricular Hypertrophy; LVDD: Left Ventricular Diastolic Function.

Discussion

In HTN patients, diastolic dysfunction can be caused by several mechanisms, including increased blood pressure, structural changes in LV, and impairment of coronary microcirculation. These factors collectively contribute to the development and progression of diastolic dysfunction in HTN patients **[11,12].** The relationship between

HTN and LVH has been extensively studied in both population-based studies and hypertensive cohorts. These studies consistently demonstrated a strong association between HTN and the development of LVH **[13,14].** The present study revealed new data on the correlation between geometry and diastolic function in a large cohort of elderly individuals in the Jinshan district of Shanghai. All participants underwent echocardiographic assessments to examine systolic and diastolic function. Importantly, integrated medical histories and cardiac biomarkers were collected and analyzed to determine the factors associated with LVDD and LVH in the elderly community. The findings of the present study indicated that 53.9% of the elderly participants had HTN. Among participants in this study, 902 were diagnosed with LVDD, of whom 541 (60%) had HTN and 361 (40%) had normotension. The average age of participants was 76±5 years old, and 72% of them were female in the LVDD group. Notably, 432 (47.9%) of LVDD patients were also diagnosed with LVH. When compared to the HTN with LVDD group, those in the normotension with LVDD group had fewer cardiovascular comorbidities, including DM, CHD, obesity, and dyslipidemia. In addition to the influence of elevated blood pressure, the presence of LVDD in the normotension group could be associated with factors, such as DM, CHD, and obesity.

Notably, LVH is considered as an adaptive response to chronic afterload stress, and it can lead to pathological changes in the structure and function of the cardiovascular system **[15].** Francesca et al. **[16]** demonstrated a high prevalence of LVH (60%) in older patients with HTN compared with younger HTN patients. Age was identified as a significant and independent factor associated with RWT. In the present study, it was found that among LVDD patients with HTN, the distribution of normal LV geometry, concentric LV remodeling, eccentric LVH, and concentric LVH was similar to that of normotensive LVDD patients. Additionally, among female participants, regardless of HTN status, the number of individuals with any of the four types of LV geometries was higher compared to males. Further analysis revealed that both LVDD patients with and without HTN showed enlargement in LVEDVI, LAVI, and LVMI, indicating that these changes in LV structure were associated with diastolic function. The correlation between LVH severity and diastolic impairment has been observed in several clinical trials, such as HTN **[17],** hypertrophic cardiomyopathy **[18],** and aortic stenosis **[19].** Francesca et al. also revealed that in older HTN patients, the relationship between cardiac morphology and diastolic function could be affected by a series of aging-associated factors **[16].**

The multivariate logistic regression analysis showed that LVDD was associated with aging, female gender, HNT, CHD, DM, obesity, and LVH. Several relevant studies demonstrated such relationship in large cohorts **[20-22].** The same result was found in the present study, where LVH was associated with a 1.352-fold higher morbidity of LVDD (95% Confidence Interval (CI): 1.122-1.688). Furthermore, multivariate logistic regression analysis indicated that LVH was significantly related to the presence of LVDD, female gender, and aging. Specifically, LVDD was associated with a 1.314-fold higher morbidity of LVH (95% CI: 1.113-1.614). Notably, LVH is predominantly a result of the adaptation to the increased cardiac afterload in HTN [23,24]. In the present study, it could be speculated that a more significant role could be played by female gender and aging in the occurrence of LVH in elderly patients with LVDD.

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