ORIGINAL ARTICLE

Left ventricular hypertrophy, abnormal ventricular geometry and relative wall thickness are associated with increased risk of stroke in hypertensive patients among the Han Chinese

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Our study aimed to explore whether left ventricular hypertrophy (LVH), abnormal LV geometry and relative wall thickness (RWT) are associated with an increased risk of stroke in a hypertensive Chinese population. This study included 462 stroke patients and 3808 non-stroke hypertensive patients. LVH was diagnosed using the criteria of LV mass $\ge 49.2 \text{ g m}^{-2.7}$ for men and 46.7 g m^{-2.7} for women. A partition value of 0.43 was used for RWT. LV geometric patterns (normal, concentric remodeling, concentric or eccentric hypertrophy) were calculated according to LVH and RWT. Logistic regression analyses were used to determine the odds ratio (OR) and 95% confidence intervals (CI) of LVH, LV geometry abnormality and RWT for stroke. Our study suggested that LVH was associated with increased stroke risk (adjusted OR, 1.52; 95% CI, 1.25–1.85; multivariate-adjusted OR, 1.43; 95% CI, 1.16–1.75) and that concentric hypertrophy carried the highest risk of stroke (adjusted OR, 1.62; 95% CI, 1.21–2.17), followed by eccentric hypertrophy (adjusted OR, 1.51; 95% CI, 1.12–2.03), with concentric remodeling ranked third (adjusted OR, 1.34; 95% CI, 1.01–1.80). RWT was associated with an increased risk of stroke and was independent of LVMI and other risk factors for stroke (adjusted OR, 3.97; 95% CI, 1.10–14.34). Our observations in Chinese patients with hypertension indicated that LVH was an important risk factor for stroke, LV geometry abnormality was related to the presence of stroke, concentric hypertrophy carried the highest risk of stroke in cases of abnormal LV geometry and that RWT was also a risk factor for stroke and was independent of LVMI and other stroke risk fa

Keywords: left ventricular geometry abnormality; left ventricular hypertrophy; risk factors; stroke

INTRODUCTION

Stroke is a major health problem worldwide and is also the leading cause of mortality and disability in the hypertensive Chinese population.¹ Previous studies have identified both left ventricular hypertrophy (LVH) and LV geometry abnormality as independent risk factors for stroke.^{2,3} However, different LV geometry abnormalities have various degrees of stroke risk; specifically, concentric hypertrophy carried the strongest risk, whereas eccentric hypertrophy ranked second. The role of concentric remodeling in mediating stroke remains controversial.^{4,5} The LV relative wall thickness (RWT) was another factor that may increase the incidence of stroke after adjustment for LV mass and has additional value in predicting stroke risk.⁴ subtypes of stroke in Chinese people are much different from those that are most common in Western populations. For example, the incidence of hemorrhagic stroke is 2–3 times higher in Chinese patients than in Whites. In addition, different ethnicities have differences in LV mass and LV geometry patterns.^{6,7} The relationships of LVH, LV geometry abnormalities and RWT with stroke in Chinese populations are not entirely elucidated. Thus, the aim of our study was to explore whether LVH, LV geometry abnormality and RWT contribute to the development of stroke in a hypertensive Chinese population.

METHODS

Study population

To date, most previous studies related to this subject have been performed in White, Black and Hispanic populations. $^{2-4}$ However, the

Details of our study protocol have been previously described.⁸ In brief, this community-based cross-sectional study was conducted in XinYang County,

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located in the middle region of China from 2004 to 2005. We used a multistage cluster sampling method to select a representative sample of rural community residents aged 40 to 75 years. A total of 13444 subjects (5270 men and 8174 women) underwent the survey, yielding a response rate of 84.9%. Of the survey respondents, 5421 hypertensive patients were identified and thoroughly examined. Hypertension was defined as having a diastolic blood pressure of \geq 90 mm Hg, systolic blood pressure of \geq 140 mm Hg, having been diagnosed with hypertension by a physician or currently taking medication for hypertension (as defined by WHO 1999). Blood pressure was measured by trained professionals with a standardized mercury sphygmomanometer, and one of three cuff sizes (regular adult, large or small) was chosen on the basis of the circumference of the participant's right arm. All participants were advised to avoid alcohol, cigarette smoking, coffee/tea and exercise for at least 30 min before their BP measurement. The average of three readings with the participant in the sitting position after at least 5 min of rest, recorded at least 30 s apart, was obtained for analysis. To obtain overnight fasting blood specimens, food and water (including antihypertensive agents) were forbidden on the day of the measurement.

The study protocol was reviewed and approved by the ethical committees of FuWai Hospital and other local hospitals. All participants gave their informed consent before they were recruited and reported themselves to be of Han nationality. All investigators were trained at the Cardiovascular Institute, Chinese Academy of Medical Science (Beijing, China) and were tested for eligibility.

Diagnostic evaluation

Three subtypes of stroke—cerebral atherosclerosis (atherothrombosis), lacunar infarction (lacunar) and intracerebral hemorrhage (hemorrhage)—were included in our present study. Other types of stroke, including transient ischemic attack, subarachnoid hemorrhage, embolic brain infarction, brain tumors and cerebrovascular malformation, and severe systemic diseases such as collagenosis, endocrine and metabolic diseases (except diabetes mellitus), inflammation, cancer of the liver or renal diseases were in the range of exclusion. The diagnosis of stroke was based on the results of strict neurological examination, computed tomography or magnetic resonance imaging tests according to the International Classification of Diseases, ninth revision.

Echocardiographic methods

Transthoracic echocardiography was performed according to a standard protocol9 including M-mode, 2-dimensional (2D) and color Doppler recordings from the parasternal long-axis and short-axis windows as well as 2D and color Doppler evaluations from the apical window to yield 2-, 3- and 4-chamber images with a HP 5500 (Phillips Medical System, Boston, MA, USA) or a HDI 3000 (ATL, Bothell, WA, USA). The transducer frequency was 2.5–3.5 MHz. Optigo echocardiographic recorders (Agilent, Boston, MA, USA) were occasionally used to screen subjects who could not visit the local study center. The echocardiographic examination was supervised by two physician echocardiographers with at least 2 years of experience. Two technicians from each center (a total of four centers) performed all the echocardiographic studies. Before the study, the technicians were trained in the echocardiographic protocol at the Cardiovascular Institute at the Chinese Academy of Medical Science. Re-scan as well as inter- and intra-observer reproducibility for M-mode measurements of cardiac dimensions was evaluated. Components of variability for left ventricular mass measurements were as follows: intraechocardiographer (7.4% from 80 paired studies), inter-echocardiographer (7.8% from 80 paired studies), intra-reader (6.9% from 300 paired studies) and inter-reader (8.8% from 300 paired studies).

Echocardiographic measurements

Correct orientation of planes for 2D and Doppler imaging was confirmed using standard procedures.¹⁰ LV internal dimensions and septal and posterior wall thicknesses were measured in up to three cardiac cycles at end-diastole and end-systole according to the American Society of Echocardiography recommendations.¹¹ When optimal orientation of the LV views could not be obtained, as is common in subjects who are overweight or over age 60, correctly oriented 2-dimensional linear dimension measurements were made following the leading edge convention of the American Society of Echocardiography. 12

Calculation of derived variables

LV mass was calculated by using the equation: $0.8 \times 1.04[(IVS + LVEDD + PW)^3 - LVEDD^3] + 0.6$, which yields values closely related (R = 0.90) to necropsy LV weight.¹³ LV mass was divided by height^{2.7} to obtain LV mass index (LVMI_{h2.7}). RWT1 (Reichek and Devereux¹⁴) was calculated by (IVS + PW)/LVEDD, and RWT2 (Reichek and Devereux¹⁴) was calculated by 2 × PW/LVEDD, where IVS is interventricular septum, PW is posterior wall and LVEDD is left ventricular end-diastolic diameter.

LVH was diagnosed using the criteria of LV mass $\geq 49.2 \, \mathrm{g \, m^{-2.7}}$ for men and 46.7 g m^{-2.7} for women.¹⁵ A partition value of 0.43 (Roman *et al.*¹⁶) was used for RWT2 and 0.45 (Reichek and Devereux¹⁴) for RWT1, respectively. Normal geometry was present when LVMI and RWT2 were normal, whereas normal LVMI and increased RWT2 identified concentric remodeling. Increased LVMI but normal RWT2 identified eccentric LV hypertrophy, and increases in both variables signified concentric LV hypertrophy.¹⁷

Statistical analysis

SPSS (Statistical Package for the Social Sciences) software version 13.0 (SPSS Inc., Chicago, IL, USA) was used for data management and statistical analysis. Data are reported as the mean \pm s.d. for continuous variables and as frequency for categorical variables. Differences between proportions were assessed by the χ^2 -test or Fisher's exact test; the difference between stroke and non-stroke groups was assessed by the independent samples *t*-test. The age- and sexadjusted and multivariate-adjusted echocardiographic characteristics were determined by general liner model (GLM). The binary logistic regression model and multivariate analysis were used to determine the odds ratio (OR) and 95% confidence intervals (CIs) of LVH, LV geometry abnormality and RWT for stroke. A two-tailed value of P < 0.05 was considered significant.

RESULTS

Clinical and echocardiographic characteristics of the study population

The patients with hypertrophic cardiomyopathy (n=8), valvular heart diseases (n=108), pulmonary hypertension (n=7) and coronary heart diseases (n=412) were excluded. All patients with complete integrated clinical and echocardiographic data were included in our study.

The clinical characteristics of the study population are described in Table 1. Male patients comprised 48.3% of the stroke group and 31.3% of the non-stroke group. The indicators including age, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure (MAP) and pulse pressure were all higher in the stroke group compared with the non-stroke group. There were no significant differences in height, body mass index, body surface area (BSA) or the prevalence of diabetes between the two groups. The echocardiographic characteristics of the study population are shown in Table 2. In addition to left ventricular end-diastolic diameter, the other echocardiographic characteristics, including posterior wall, interventricular septum, LV mass, LVMI_{h2.7}, LVMI_{BSA}, RWT1 and RWT2, were all higher in the stroke group than in the non-stroke group, regardless of the use of unadjusted or age- and sex-adjusted and multivariate-adjusted methods.

LVH and risk of stroke

LVH was associated with increased stroke risk (age- and sex- adjusted OR, 1.52; 95% CI, 1.25–1.85; multivariate-adjusted OR, 1.43; 95% CI, 1.16–1.75, in Table 3). This tendency was also observed in males and females. In age strata, LVH was not a risk factor for stroke in the

40-55-year age group, whereas this factor was associated with increased stroke risk in the 55-74-year age group.

LV geometry and risk of stroke

The distribution of LV geometry patterns is described in Table 4 and Figure 1. Concentric hypertrophy (28.54% vs. 21.76%; P = 0.001) was higher in the stroke group than in the non-stroke group. Eccentric hypertrophy and concentric remodeling seem to be higher in the stroke group compared with that in the non-stroke group, but there is no statistical significance (21.92% vs. 19.98%; P = 0.36); (25.57% vs. 24.54%; P = 0.18). The normal geometry pattern was more common in the non-stroke group (33.72% vs. 23.97%; P < 0.001).

Concentric hypertrophy carried the highest risk of stroke (unadjusted OR 1.93, 95% CI, 1.48–2.53; adjusted OR, 1.62, 95% CI, 1.21– 2.17), followed by eccentric hypertrophy (unadjusted OR, 1.61, 95% CI, 1.08–2.54; adjusted OR, 1.51, 95% CI, 1.12–2.03), and concentric

Table 1 Clinical characteristics of the study population

Clinical characteristics	<i>Stroke (</i> n = 462)	Non-stroke (n = 3808)	P-value
Age (years)	60.70±7.53	58.37±8.07	< 0.001
male (%)	48.3%	31.3%	< 0.001
SBP (mm Hg)	168.85 ± 23.88	165.01 ± 22.47	0.001
DBP (mm Hg)	99.54 ± 12.34	97.74 ± 11.67	0.002
MABP (mm Hg)	122.64 ± 14.43	120.16 ± 13.52	< 0.001
Pulse pressure (mm Hg)	69.31±19.38	67.27±18.53	0.026
Diabetes, %	6.1	4.7	0.21
Height, cm	158.38 ± 7.72	157.66±7.95	0.063
BMI, kgm ⁻²	26.26±3.80	26.25±3.68	0.936
BSA, m ²	1.67 ± 0.16	1571.66.66±7.950.17	0.13
Glucose (mmoll ⁻¹)	5.64 ± 1.67	5.66 ± 1.81	0.27
Triglyceride (mmol I $^{-1}$)	1.67 ± 1.42	1.72 ± 1.26	0.19
Cholesterol (mmol I ⁻¹)	5.53 ± 1.14	5.49 ± 1.13	0.33
HDL-C (mmol I ⁻¹)	1.58 ± 0.34	1.61 ± 0.36	0.21
LDL-C (mmol I ⁻¹)	3.24 ± 0.87	3.18 ± 0.92	0.35
BUN (mmoll ^{-1})	6.03 ± 2.13	5.53 ± 1.79	0.15
$\operatorname{Ccr}(\operatorname{mlmin}^{-1})$	96.71±26.8	97.2±31.5	0.17

Abbreviations: BMI, body mass index; BUN, blood urea nitrogen; CAD, coronary artery disease; Ccr, creatinine clearance rate; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; MABP, mean arterial blood pressure; SBP, systolic blood pressure. remodeling ranked third (unadjusted OR, 1.47, 95% CI, 1.12–1.93; adjusted OR, 1.34, 95% CI, 1.01–1.80). Concentric hypertrophy was found to increase stroke risk in both males and females in unadjusted and adjusted models. Eccentric hypertrophy was associated with increased stroke risk in both sexes in unadjusted models, but it was only associated with stroke risk in females in the adjusted model, while concentric remodeling was associated with stroke risk in females in all models.

RWT and risk of stroke

RWT was associated with an increased stroke risk after adjustment for LVMI. In the univariate model, the OR was 5.34 (95% CI 1.51–18.91); in the multivariate model, which was adjusted for age, sex, systolic blood pressure, body mass index, serum glucose, triglyceride, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood urea nitrogen, serum creatinine, and LVMI, the OR was 3.97 (95% CI 1.10–14.34). No interaction with regard to stroke risk was found between RWT and LVMI (P = 0.78 unadjusted).

DISCUSSION

We conducted our study in a rural area of China, namely, in Xinyang City, Henan Province, the population of which is different from most

Table 3 Association between left ventricular hypertrophy and
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		LVH	
		Age- and	
	Unadjusted	sex-adjusted	Multivariate-adjusted
	OR (95% CI)	OR (95% CI)	ORª (95% CI)
Whole group	1.49 (1.23, 1.80)	1.52 (1.25, 1.85)	1.43 (1.16, 1.75)
Male	1.76 (1.32, 2.34)	1.71 (1.28, 2.29)	1.59 (1.17, 2.16)
Female	1.46 (1.12, 1.90)	1.40 (1.06, 1.82)	1.31 (1.00, 1.73)
Age 40–55 years	1.44 (0.97, 2.15)	1.45 (0.97, 2.16)	1.30 (0.84, 1.99)
Age 55–74 years	1.40 (1.12, 1.75)	1.54 (1.23, 1.93)	1.48 (1.16, 1.88)

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio; LVH, left ventricular hypertrophy.

^aAdjusted for age, sex, systolic blood pressure, diastolic blood pressure, body mass index, serum glucose, triglyceride, cholesterol, HDL cholesterol, LDL cholesterol, blood urea nitrogen, creatinine clearance rate.

Table 2 Unadjusted and age-, sex-adjusted and multivariate-adjusted echocardiographic characteristics of the study population

	Unadjusted			Age- and sex-adjusted			Multivatriate-adjusted ^a		
	Stroke	Non-stroke		Stroke	Non-stroke		Non-stroke		
	(n = 462)	(n = 3808)	P-value	(n = 462)	(n = 3808)	P-value	<i>Stroke</i> (n = 462)	(n = 3808)	P-value
LVIDD, mm	45.86±5.23	45.44±5.10	0.10	45.6 (45.2, 46.1)	45.5 (45.3, 45.6)	0.55	45.5 (45.1, 46.0)	45.5 (45.3, 45.6)	0.82
PWTd, mm	10.11 ± 1.43	9.72±1.34	< 0.001	10.0 (9.9, 10.1)	9.7 (9.7, 9.8)	< 0.001	9.9 (9.8, 10.0)	9.7 (9.7, 9.8)	0.001
IVSd, mm	10.47 ± 1.60	9.98±1.58	< 0.001	10.3 (10.2, 10.5)	10.0 (9.9, 10.0)	< 0.001	10.2 (10.1, 10.4)	10.0 (9.9, 10.0)	0.001
LV mass, g	170.62±46.36	158.52±43.68	< 0.001	166.7 (162.8, 170.6)	159.0 (157.7, 160.3)	< 0.001	164.3 (160.5, 168.1)	159.1 (157.8, 160.4)	0.01
LVMI _{h2.7}	49.29±12.68	46.43 ± 12.47	< 0.001	49.0 (47.9, 50.2)	46.5 (46.1, 46.9)	< 0.001	48.4 (47.3, 49.5)	46.6 (46.2, 46.9)	0.002
LVMI _{BSA}	101.79±25.15	95.36 ± 24.27	< 0.001	100.1 (97.9, 102.3)	95.6 (94.8, 96.3)	< 0.001	99.2 (97.0, 101.4)	95.7 (94.9, 96.4)	0.003
RWTm	0.45±0.082	0.44 ± 0.078	< 0.001	0.45 (0.44, 0.46)	0.44 (0.44, 0.44)	0.002	0.45 (0.44, 0.46)	0.44 (0.44, 0.44)	0.018
RWTp	0.45 ± 0.078	0.43 ± 0.075	< 0.001	0.44 (0.44, 0.45)	0.43 (0.43, 0.44)	0.003	0.44 (0.43,0.45)	0.43 (0.43, 0.44)	0.004

Abbreviations: IVSd, end-diastolic interventricular septal thickness; LVIDD, end-diastolic LV internal dimension; LVMI_{BSA}, left ventricular mass index divided by body mass index; LVMI_h, left ventricular mass index divided by height2.7; PWTd, end-diastolic posterior wall thickness; RWT_m, relative wall thickness calculated by (IVS + PW)/LVEDD; RWT_p, relative wall thickness calculated by 0.2 × PWTd/UVDD.

^aÁdjusted for age, sex, systolic blood pressure, diastolic blood pressure, body mass index, serum glucose, triglyceride, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood urea nitrogen, creatinine clearance rate.

	Concentric hypertrophy (n $=$ 964)		Eccentric hypertrophy (n = 862)		Concentric remodeling (n = 1054)		
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	
	OR (95% CI)	ORª (95% CI)	OR (95% CI)	ORª (95% CI)	OR (95% CI)	ORª (95% CI)	
Whole group	1.93 (1.48, 2.53)	1.62 (1.21, 2.17)	1.61 (1.08, 2.54)	1.51 (1.12, 2.03)	1.47 (1.12, 1.93)	1.34 (1.01, 1.80)	
Male	2.32 (1.57, 3.44)	1.61 (1.04, 2.51)	1.66 (1.08, 2.54)	1.47 (0.93, 2.31)#	1.33 (0.89, 1.97)#	1.20 (0.79, 1.81)#	
Female	1.89 (1.30, 2.75)	1.68 (1.13, 2.50)	1.76 (1.19, 2.60)	1.69 (1.13, 2.54)	1.61 (1.09, 2.37)	1.54 (1.03, 2.30)	

Table 4 Association between left ventricular geometry abnormality and stroke

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio.

^aAdjusted for age, sex, systolic blood pressure, diastolic blood pressure, body mass index, serum glucose, triglyceride, cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood urea nitrogen, creatinine clearance rate.

[#]P>0.05.

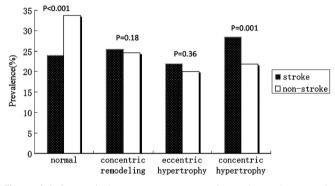


Figure 1 Left ventricular geometry patterns in stroke and non-stroke populations.

previous studies, which were generally conducted in urban areas. There are almost 0.7 billion people living in rural areas in China and whose lifestyle and medical and economic conditions are much different from those of people who live in the major cities. Henan Province is an economically underdeveloped province in China, and the local people have less medical knowledge and lower rates of therapy and control of hypertension. To the best of our knowledge, the present study is the first large-scale study to evaluate the association of LVH, LV geometry abnormality and RWT with the risk of stroke in patients with hypertension from a rural population in China.

In the present large, community-based cross-sectional study, LVH was associated with increased stroke risk in the whole group and in males and females; LV geometry abnormality was also related to the presence of stroke; concentric hypertrophy carried the highest risk of stroke in the abnormal LV geometry; RWT was a risk factor for stroke and was independent of LVMI and other stroke risk factors.

The results of our study suggested that LVH is associated with increased stroke risk in Chinese people with hypertension. Some early studies have indicated that LVH may be considered a potent sign of generalized preclinical disease in hypertensive patients. Verdecchia *et al.*¹⁸ also demonstrated the association between LVH and symptomatic cerebrovascular disease in a White population. The study by Di Tullio *et al.*¹⁹ showed that LVH is strongly associated with ischemic stroke in all age, sex and race-ethnic subgroups. Together, these findings indicate that more attention needs to be directed toward maintaining cerebral circulation in patients with LV hypertrophy, and echocardiographic examinations should be carried out regularly in the hypertensive population to optimize the clinical management of these patients.

LV geometry abnormality was also related to the presence of stroke. Concentric hypertrophy carried the highest risk of stroke in both male and female patients. Eccentric hypertrophy and concentric remodeling were also associated with stroke risk in the whole population and in females. These results further confirmed a previous observation that patients with concentric LV hypertrophy have the greatest risk of mortality, followed by those with eccentric LV hypertrophy.²⁰ In addition, our results showed that the female patients with geometric abnormalities were more susceptible to developing stroke. However, Taylor *et al.*²¹ reported that the association between concentric LV hypertrophy and mortality risk remained only in men after adjustments for baseline differences in cardiovascular disease risk factors and LV mass. This incongruent finding may be due to differences in patient race or study end points.

RWT was associated with increased stroke risk after adjustment for LVMI and other risk factors for stroke, suggesting that RWT is a risk factor for stroke independent of LVMI and other stroke risk factors. This result is consistent with the finding from the study by Di Tullio *et al.*,¹⁹ which showed that increased LV RWT imparts an increased stroke risk after adjustment for LV mass and is of additional value in stroke risk prediction.

Study strength and limitation

Our study examined a large population of patients with hypertension. To date, this study includes the largest number of echocardiographic evaluations of LV mass. In addition, our study subjects are community-based hypertensive patients living in a rural area, which could diminish selection bias and serve as a better representation of the Chinese hypertensive population. Finally, echocardiographic estimates of left ventricular mass are more sensitive and specific than those estimates obtained by ECG.

There are still limitations in our current study. First, the indexation methods and partition values of LVH, LV geometry abnormality and RWT were derived from previous studies and have not been prospectively validated using independent data. Second, because many male rural residents have been living away from home to work in cities, more female subjects were recruited into this study. Third, our study is cross-sectional and requires long-term follow-up to determine the predictive value of LVH and LV geometry abnormality for cardiovascular and cerebrovascular events.

In conclusion, our observations in Chinese patients with hypertension indicated that LVH was an important risk factor for stroke. LV geometry abnormality was also related to the presence of stroke, and concentric hypertrophy carried the highest risk of stroke in the abnormal LV geometry. RWT was also a risk factor for stroke and was independent of LVMI and other stroke risk factors. Our results suggest that effective control of LVH and LV geometry abnormality may be important targets for preventing stroke in hypertensive populations.

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