

Full Length Research Paper

# Patterns of left ventricular hypertrophy and geometry in newly diagnosed hypertensive adults in Northern Nigerians

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In hypertensives, left ventricular hypertrophy predicts increased cardiovascular morbidity and mortality. Adding to this burden is abnormality of left ventricular (LV) geometry. Knowledge of the left ventricular geometric patterns in our newly diagnosed hypertensives may have some prognostic significance. One hundred (100) newly diagnosed hypertensives (61 males and 39 females) and 78 normotensives (46 males and 32 females) were recruited for the study. All were clinically evaluated and an echocardiographic examination performed. Mean ages for the study subjects and controls were  $51.40 \pm 11.60$  and  $51.50 \pm 11.50$  years respectively ( $P = 0.47$ ). Only 24% of the hypertensives had normal geometry with 76% being abnormal. Normal geometry was found in 63% of the controls with 37% being abnormal. Statistical significance was noticed when the geometric patterns of the hypertensive and controls were compared ( $p$  value  $< 0.001$ ). This study showed that only 24% of our hypertensives had normal LV geometric pattern at diagnosis while over 35% of the controls had abnormal geometry. Early diagnosis and aggressive treatment to control hypertension should be taken with all seriousness.

**Key Words:** Hypertension, left ventricular hypertrophy, geometry, adults, Nigerians.

## INTRODUCTION

Left ventricular hypertrophy (LVH), or increased LV mass, is a risk factor for cardiovascular diseases. Echocardiographic LVH is associated with cardiovascular morbidity and mortality, as well as all-cause mortality (Di Tullio et al., 2003; Ganau et al., 1992; Koren et al., 1991). The risk increase is independent of other cardiovascular risk factors, including arterial hypertension (Haider et al., 1998). Recently, there have been reports of incremental risk associated with abnormal LV geometry beyond the simple LV mass increase. From LV mass and relative wall thickness (RWT), 3 abnormal geometric patterns - concentric hypertrophy, eccentric hypertrophy, and concentric remodeling - are identified that appear to carry different risks for cardiovascular events (Haider et al., 1998; Schillaci et al., 2000; Ganau et al., 1992). Concentric hypertrophy (increase in both LV mass and RWT) carries the highest risk, followed by eccentric hypertrophy (increased LV mass, normal RWT)

(Verdecchia et al., 1995). The independent risk of an isolated RWT increase (concentric remodeling) is controversial (Gardin et al., 2001; Gerds et al., 2008). Racial difference and prognosis of the different geometric patterns in hypertension had also been established (Mayet et al., 1994; Dunn et al., 1983). These studies were however mainly reported from African - Americans and other ethnic groups. Data from Nigeria is from the Western part of the country, with literature being scant from the North. This study was carried out to determine the type and prevalence of left ventricular geometric patterns in our newly diagnosed hypertensive patients as seen from a Northern Nigerian Tertiary institution.

## Study population

One hundred (100) consecutive, newly presenting adult hypertensive subjects aged 30 and above seen at the cardiac clinic and / or the general outpatient department of Ahmadu Bello University Teaching Hospital, Zaria were recruited over a period nine months (Jun 2007 - March 2008). The controls were recruited from among hospital

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**Table 1.** Clinical and physical characteristics of the study group.

Variable	Status		
	Hypertensives	Controls	P value
Age (years, Mean $\pm$ SD)	51.4 $\pm$ 11.6	51.5 $\pm$ 11.5	0.47
Sex (Male/Female)	61/36	46/32	
Height (m, Mean $\pm$ SD)	1.63 $\pm$ 0.09	1.66 $\pm$ 0.08	0.01
Weight (kg, Mean $\pm$ SD)	64.8 $\pm$ 14.0	65.4 $\pm$ 13.0	0.39
BMI (kg/m <sup>2</sup> , Mean $\pm$ SD)	24.6 $\pm$ 5.0	22.9 $\pm$ 3.0	0.003
WHR (Mean $\pm$ SD)	0.96 $\pm$ 0.07	0.89 $\pm$ 0.05	0.0002
SBP (mmHg, Mean $\pm$ SD)	184 $\pm$ 35	125 $\pm$ 10	0.0001
DBP (mmHg, Mean $\pm$ SD)	117 $\pm$ 21	79 $\pm$ 6	0.0003
MAP (mmHg, Mean $\pm$ SD)	139 $\pm$ 24	94 $\pm$ 7	0.0003

BMI = body mass index, WHR = waist to hip ratio, SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP = mean arterial blood pressure.

staff, relatives of hospital patients and the community, who are not hypertensives and had no family history of hypertension. Ethical approval was obtained from the ethical review committee of our institution and informed consent was obtained from the study participants. Exclusion criteria include diabetes, chronic renal failure, valvular heart disease and /or ischemic heart. Blood pressure measurements were obtained according to standard guidelines (American Society of Hypertension 1992) with a mercury sphygmomanometer (Accusson's London). Arterial hypertension was defined by blood pressure 140/90 mm Hg (average of 2 measurements) using the JNC VII definition (Chobanian et al., 2003).

### Echocardiography

The echocardiographic examinations were performed with the Aloka SSD 4000 machine with 3.5 MHz transducer. The echocardiographic measurements were performed by two of the authors (DSS and OAI) according to the recommendation of the American Society of Echocardiography (Sahn et al., 1978). LV mass was calculated from the formula: LV mass (g) = 1.04 [(IVSd + LVIDd + PWTd)<sup>3</sup> - (LVIDd)<sup>3</sup>] + 14(14) and then indexed to body surface area. Left ventricular hypertrophy (LVH) was considered present if the left ventricular mass index [LVMI] is > 134 g/m<sup>2</sup> in males and > 110 g/m<sup>2</sup> in females. Relative wall thickness (RWT) was calculated as 2  $\times$  PWTd/LVIDd. Increased relative wall thickness was present when RWT 0.42 (Ganaue et al., 1992). LV geometry was defined using RWT and LV mass index (LVMI) as: Normal Geometry (Normal LVMI and RWT); Concentric Remodeling: (Normal LVMI and Increased RWT); Concentric LVH: (Increased LVMI and RWT 0.42) and Eccentric LVH: Increased LVMI and RWT < 0.42 (Ganaue et al., 1992).

### Data analysis

Statistical analysis was performed with SPSS software

version 11.0 (SPSS Inc., Chicago, Illinois). Data are reported as mean  $\pm$  SD for continuous variables and as frequency for categorical variables. Differences between proportions were assessed by  $\chi^2$  test differences between mean values, by unpaired Student's *t* test. A 2-tailed value of *P* = 0.05 was considered significant.

### RESULTS

One hundred hypertensives (61 males and 39 females) and 78 normotensives (46 males and 32 females) aged 30 to 79 years were recruited for the study. The clinical and physical characteristics of the subjects are as shown in Table 1. There was no significant difference in the ages of the groups. But the body mass index (BMI), weight, height, waist to hip ratio, systolic, diastolic, mean arterial and pulse pressures of the hypertensive subjects were significantly more than in the control group (Table 1). All echocardiographic parameters were significant in the hypertensives compared to the controls (Table 2). There were also significant differences in systolic, diastolic and mean arterial pressures in all the different geometric patterns. The systolic, diastolic and mean arterial pressures were higher in concentric hypertrophy group compared to the rest (Table 3). Table 4 showed that septal and posterior wall thicknesses, LV mass, RWT and LVMI were significantly different among the various geometric patterns. Septal and posterior wall thicknesses were significantly larger in concentric hypertrophy when compared with the other geometric patterns.

### DISCUSSION

Framingham Study and other population - based studies have shown that increased left ventricular (LV) mass, also referred to as left ventricular hypertrophy (LVH), is an independent predictor of cardiovascular events in population - based studies using electrocardiograms or echocardiography to define LVH

**Table 2.** Echocardiographic characteristics of the study group

Variable	status		
	Hypertensives (n = 100)	Controls (n = 78)	P value
IVSd (cm, Mean ± SD)	1.34 ± 0.44	1.1 ± 0.22	0.0003
LVIDd (cm, Mean ± SD)	5.2 ± 0.73	4.4 ± 0.64	0.0003
LVPWd (cm, Mean ± SD)	1.1 ± 0.33	0.91 ± 0.22	0.0003
LVM (grm, Mean ± SD)	291.0 ± 130	166.0 ± 54.0	0.0004
LVMI (g/m <sup>2</sup> , Mean ± SD)	178.0 ± 83	93.0 ± 29	0.0007

LV = left ventricular geometry, LVH = left ventricular hypertrophy, SD = standard deviation, grm = grams, g/m<sup>2</sup> = grams per meter squared

**Table 3.** Comparison of Independent Variables by LV Geometry

Variable	Concentric	Eccentric	Concentric	Normal	P value
	LVH	LVH	Remodeling	Geometry	
	(n = 37)	(n = 43)	(n = 29)	(n = 69)	
Age (years)	51.14±10.9	50.30±11.03	50.42±11.33	50.71±12.6	NS
Weight (kg)	65.7±13.3	65.12±13.7	64.6±13.4	64.9±13.0	NS
Height (m)	1.63±0.10	1.63±0.08	1.65±0.10	1.66±0.08	0.03
BMI (kg/m <sup>2</sup> )	25.14±5.42	24.16±4.24	23.28±4.71	23.15±3.34	0.003
SBP (mmHg)	191.8±42.4	174.0±34.0	139.6±26.0	133.5±29.5	0.0002
DBP (mmHg)	119.0±26.2	111.3±21.8	89.2±21.4	86.2±18.0	0.0001
MAP (mmHg)	142.6±30.0	132.8±26.0	108.0±18	102.2±20.0	0.0003
PP (mmHg)	72.6±28.0	64.0±17.2	50.0±18.0	48.4±15.0	0.0002

BMI = body mass index; SBP = systolic blood pressure, DBP = diastolic blood pressure, MAP = mean arterial blood pressure and PP = pulse pressure.

**Table 4.** Echocardiographic characteristics of the different geometric patterns.

Variable	Concentric LVH	Eccentric LVH	Concentric remodeling	Normal geometry	P value
	(n = 37)	(n = 43)	(n = 29)	(n = 69)	
IVSd (cm, Mean ± SD)	1.58 ± 0.47	1.25 ± 0.19	1.12 ± 0.45	1.03 ± 0.23	0.002
LVIDd (cm, Mean ± SD)	5.09 ± 0.72	5.50 ± 0.53	4.47 ± 0.58	3.93 ± 0.56	0.003
LVPWd (cm, Mean ± SD)	1.42 ± 0.25	1.00 ± 0.13	1.11 ± 0.31	0.81 ± 0.13	0.0004
RWT	0.59 ± 0.14	0.46 ± 0.06	0.56 ± 0.11	0.36 ± 0.06	0.0001
LVM (g, Mean ± SD)	379.0 ± 138.8	292.0 ± 74.8	158.7 ± 41.0	155.7 ± 41.2	0.004
LVMI (g/m <sup>2</sup> , Mean ± SD)	234.3 ± 91.9	177.1 ± 38.1	90.2 ± 22.0	87.4 ± 22.4	0.0003

(Devereux and Reichek 1977, Fox et al., 2004; Savage et al., 1987). Various geometric patterns have associated with arterial systemic hypertension (Cunha et al., 2001). These geometric changes of the ventricle, termed remodeling, have been investigated primarily by echocardiography in relationship to cardiovascular events (Shipilova et al., 2003; Levy et al., 1990; Mazza et al., 2005; Katz 1990); and the increase risk of cardiovascular events with LVH depends on the type of geometry (Lauer et al., 1991). This risk increases to as much as 30 % with concentric LVH compared to 15% with concentric remodeling (Shipilova et al., 2003). In our study, more

than 75 % of the hypertensives had altered left ventricular geometry with concentric LVH constituting 37%. Studies carried out in Europe, Brazil and United States (Cunha et al., 2001; Shipilova et al., 2003; Roman et al., 1996) showed different frequencies for the various LV geometric patterns with eccentric hypertrophy predominating. This may be influenced by ethnicity, environment and other factors such as coronary artery disease. However, African - Americans (Fox et al., 2004.) tend to have more of concentric hypertrophy as we observed in our study. LVH is associated with multiple factors, such as increased age, blood pressure, and diabetes (Tsang et

al., 2003); resulting in increased stiffness of the left ventricle. Some authors have observed that age have a profound effect on left ventricular structure and geometric patterns (Tsang et al., 2003; Sumimoto et al., 1995; Koren et al., 1993) with concentric hypertrophy and concentric remodelling increasing with age; we noticed no such relationship in our study, even though, over 55% of our patients are in their 6<sup>th</sup> decade of life. However, other factors such as high blood pressure, over weight and wide pulse pressure together with environment influence may explain our observation. RWT and LVM are higher in the blacks than whites (27, 28 and 29) when left ventricular structure and function are compared. This may explain the observed age related changes in LV geometric patterns observed in Caucasians. We also observed abnormal geometry in 37% of our controls, with concentric remodeling; concentric and eccentric hypertrophy constituting 27, 3 and 7% respectively. This observation may be explained in terms of the difficulty in getting correct and accurate information in our environment due to low literacy level and ignorance.

Secondly, occurrence of normal geometry tends to decrease with age, with increased frequency of concentric hypertrophy and concentric remodeling as age advances (Shipilova et al., 2003; Tsang et al, 2003; Sumimoto et al., 1995). Interestingly, 23% of our patients had a normal LV geometry which compares to the study of Aje et al. (2006).

### Clinical relevance

Concentric hypertrophy had the highest adverse cardiovascular outcomes (in terms of morbidity and death) compared to eccentric and concentric remodeling (Gerdtts et al., 2008). Majority of our hypertensives had concentric type. Muiesan et al (2004) made a similar observation in their patients and implicate concentric LVH as a dangerous adaptive pattern to systemic hypertension. On the other hand, some workers reported the clinical relevance of the other types of geometric patterns due to their prognostic values in especially clinical settings (Verdecchia et al., 1995; de Simone 2000). Increased incidence of arrhythmias, systolic and diastolic dysfunction, increased risk of CV events (mainly stroke) and reduced coronary reserve are some of the adverse consequences reported in patients with hypertension and LVH (Gerdtts et al., 2008; Opadijo et al., 2003; Slama et al., 2002; Pichard et al., 1981; MacMahon et al., 1986; Dahlöf et al., 1992; Schmieder et al., 1996). Our patients we believe are not exempt from these complications. However, non - pharmacological and pharmacological interventions were reported to cause regression of left ventricular wall thickness and mass; and reduction of left ventricular mass was also reported to lead to improvement of LV filling and mid - wall fractional shortening (Pichard et al., 1986; Schmieder et al., 1996). This has been shown to decrease cardiovascular

morbidity and mortality with consequent improvement of coronary reserve. This therefore indicates that antihypertensive therapy ought to target ventricular geometry as well as mass.

### Conclusion

Concentric left ventricular hypertrophy is still the commonest geometric pattern seen in our untreated hypertensives compared to concentric remodeling and eccentric types. Establishment of its significance in these indigenous Africans could however be determined by a longitudinal study.

**Competing interests:** The author(s) declare that they have no competing interests.

**Authors' contributions:** IMS conceived the study, study design, analyzed the data and drafted the manuscript. OAI, GSB and DSS participated in doing echocardiographic measurements. All authors read and approved the final manuscript.

### REFERENCES

- Di Tullio MR, Zwas RD, Sacco RL, Sciacca RR, Homma S (2003). Left Ventricular Mass and Geometry and the Risk of Ischemic Stroke. *Stroke* 34: 2380-2386.
- Ganau A, Devereux RB, Roman MT, de Simone G, Pickering TG, Saba PS, Vargin P, Simongiri I, Laragh JH (1992). Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. *J. Am. Coll. Cardiol.* 19: 1550-1558.
- Koren MJ, Devereux RB, Casale PN, Savage DD, Laragh JH (1991). Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. *Ann. Intern. Med.* 114: 345-352.
- Haider AW, Larson MG, Benjamin EJ, Levy D (1998). Increased left ventricular mass and hypertrophy are associated with increased risk for sudden death. *J. Am. Coll. Cardiol.* 32: 1454-1459.
- Schillaci G, Verdecchia P, Porcellati G, Cuccurullo O, Cosco C, Perticone F (2000). Continuous relation between left ventricular mass and cardiovascular risk in essential hypertension. *Hypertension.* 35: 580-586.
- Ganau A, Devereux RB, Roman MJ, De Simone G, Pickering TG, Saba PS, Vargiu P, Simongini I, Laragh JH (1992). Patterns of left ventricular hypertrophy and geometric remodeling in essential hypertension. *J. Am. Coll. Cardiol.* 19: 1550-1558.
- Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Santucci A, Santucci C, Reboldi G, Porcellati C (1995). Adverse prognostic significance of concentric remodeling of the left ventricle in hypertensive patients with normal left ventricular mass. *J. Am. Coll. Cardiol.* 25: 871-878.
- Gardin JM, McClelland R, Kitzman D, Lima JA, Bommer W, Klopfenstein HS, Wong ND, Smith VE, Gottdiener J (2001). M-mode echocardiographic predictors of six- to seven-year incidence of coronary artery disease, stroke, congestive heart failure and mortality in an elderly cohort (The Cardiovascular Health Study). *Am. J. Cardiol.* 87: 1051-1057.
- Gerdtts E, Cramariuc D, de Simone G, Wachtell K, Dahlöf B, Devereux RB (2008). Impact of left ventricular geometry on prognosis in hypertensive patients with left ventricular hypertrophy (the LIFE study). *Eur. J. Echocardiogr.* 9(6): 809-815.
- Mayet J, Shahi M, Foale RA, Poulter NR, Sever PS, Mc GTSA (1994). Racial differences in cardiac structure and function in essential

- hypertension. *BMJ* 308: 1011 – 1014.
- Dunn FG, Oigman W, Sungaard – Riise K, Messerli FH, Ventura H, Reisin E, Froehlich ED (1983). Racial differences in cardiac adaptation to essential hypertension determined by echocardiographic indexes. *J. Am. Coll. Cardiol.* 1: 1348–1351.
- American Society of Hypertension (1992). Recommendations for routine blood pressure measurement by indirect cuff sphygmomanometer. *Am. J. Hypertens.* 5: 207-209.
- Chobanian AV, Bakris GL, Black HR (2003). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* ; 289(19): 2560-2572
- Sahn DJ, DeMaria A, Kisslo J, Weyman A (1978). Recommendations regarding Quantitation in M-mode Echocardiography. Results of a survey of Echocardiographic measurements. *Circulation* 56:1072-1083.
- Devereux RB, Reichek N (1977). Echocardiographic determination of left ventricular mass in man: Anatomic validation of the method. *Circulation* 55(4): 613–618.
- Fox E, Taylor H, Andrew M, Han H, Mohamed E, Garrison R, Skelton T (2004). Body mass index and blood pressure influences on left ventricular mass and geometry in African Americans. The Atherosclerotic Risk in Communities (ARIC) Study. *Hypertension* 44: 55-60.
- Savage DD, Garrison RJ, Kannel WB, Levy D, Anderson SJ, Stokes J, Feinleib M, Castelli WP (1987). The spectrum of left ventricular hypertrophy in a general population sample: the Framingham Study. *Circulation* 75: 126-133.
- Cunha DM, da Cunha AB, Martins WA, Pinheiro LA, Romeo LJ, de Moraes AV, Morcerf FP (2001). Echocardiographic assessment of the different left ventricular geometric patterns in hypertensive patients. *Arq Bras. Cardiol.* 76: 15-28.
- Shipilova T, Pshenichnikov I, Kaik J, Volozh O, Abina J, Kalev M, Lass J, Meigas K (2003). Echocardiographic assessment of the different left ventricular geometric patterns in middle-aged men and women in Tallinn. *Blood Press* 12: 284-290.
- Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP (1990). Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. *N. Engl. J. Med.* 322: 1561–6.
- Mazza A, Tikhonoff V, Casiglia E, Pessina AC (2005). Predictors of congestive heart failure mortality in elderly people from the general population. *Int. Heart J.* 46: 419–31.
- Katz AM (1990). Cardiomyopathy of overload. A major determinant of prognosis in congestive heart failure. *N. Engl. J. Med.* 322: 100–110.
- Lauer MS, Anderson KM, Levy D (1991). Influence of contemporary versus 30-year blood pressure levels on left ventricular mass and geometry: the Framingham Heart Study. *J. Am. Coll. Cardiol.* 18: 1287–1294.
- Roman MJ, Pickering TG, Schwartz JE, Pini R, Devereux RB (1996). Relation of arterial structure and function to left ventricular geometric patterns in hypertensive adults. *J. Am. Coll. Cardiol.* 28: 751-756.
- Tsang TS, Barnes ME, Gersh BJ (2003). Prediction of risk for first age-related cardiovascular events in an elderly population: the incremental value of echocardiography. *J. Am. Coll. Cardiol.* 42: 1199–1205.
- Sumimoto T, Mukai M, Murakami E, Kokubu T, Lin M, Shigematsu Y, Hamada M, Hiwada K (1995). Effect of age on left ventricular geometric patterns in hypertensive patients. *J. Hypertens.* 13: 1813-1817.
- Koren MJ, Mensah GA, Blake J, Laragh JH, Devereux RB (1993). Comparison of left ventricular mass and geometry in black and white patients with essential hypertension. *Am. J. Hypertens.* 6: 815-823.
- Hinderliter AL, Blumenthal JA, Waugh R, Chilukuri M, Sherwood A (2004). Ethnic differences in left ventricular structure: relations to hemodynamics and diurnal blood pressure variation. *Am. J. Hypertens.* 17: 49.
- de Simone G, Daniels SR, Kimball TR, Roman MJ, Romano C, Chinali M, Galderisi M, Devereux RB (2005). Evaluation of concentric left ventricular geometry in humans: evidence for age-related systematic underestimation. *Hypertension* 45: 64-68.
- Aje A, Adebisi AA, Oladapo O, Dada A, Ogah OS, Ojji DB, Falase AO (2006). Left Ventricular Geometric Patterns in newly presenting Nigerian Hypertensives: An Echocardiographic Study. *BMC Cardiovascular Disorders* 6: 4.
- Muesan ML, Salvetti M, Monteduro C, Bonzi B, Paini A, Viola S, Poisa P, Rizzoni D, Castellano M, Agabiti-Rosei E (2004). Left ventricular concentric geometry during treatment adversely affects cardiovascular prognosis in hypertensive patients. *Hypertension* 43: 731-738.
- Verdecchia P, Schillaci G, Borgioni C, Ciucci A, Battistelli M, Bartoccini C, Santucci A, Santucci C, Reboldi G, Porcellati C (1995). Adverse prognostic significance of concentric remodeling of the left ventricle in hypertensive patients with normal left ventricular mass. *J. Am. Coll. Cardiol.* 25: 871-878.
- de Simone G (2000). Concentric or eccentric hypertrophy: how clinically relevant is the difference? *Hypertension* 43: 714-715.
- Opadijo OG, Omotoso ABO, Araoye MA (2003). Ventricular Arrhythmias: QT prolongation and left ventricular hypertrophy in Adults Nigerians with hypertension. *Nig. Postgrad. Med. J.* 10(2): 76 – 78.
- Slama M, Susic D, Varagic J, Froehlich ED (2002). Diastolic dysfunction in hypertension. *Curr. Opin. Cardiol.* 17: 368-373.
- Pichard AD, Gorlin R, Smith H, Ambrose J, Meller J (1981). Coronary flow studies in patients with left ventricular hypertrophy of the hypertensive type. Evidence for an impaired coronary vascular reserve. *Am. J. Cardiol.* 47: 547-554.
- MacMahon SW, Wilcken DE, Macdonald GJ (1986). The effect of weight reduction on left ventricular mass. A randomized controlled trial in young, overweight hypertensive patients. *N. Engl. J. Med.* 314: 334-339.
- Dahlöf B, Pennert K, Hansson L (1992). Reversal of left ventricular hypertrophy in hypertensive patients. A Meta analysis of 109 treatment studies. *Am. J. Hypertens.* 5: 95-110.
- Schmieder RE, Martus P, Klingbeil A (1996). Reversal of left ventricular hypertrophy in essential hypertension. A meta-analysis of randomized double-blind studies. *JAMA* 275:1507-1513.