Published in final edited form as:
J Hypertens. 2008 September ; 26(9): 1868–1874. doi:10.1097/HJH.0b013e3283050899.

Left ventricular mass and incident hypertension in individuals with initial optimal blood pressure:

The Strong Heart Study

Giovanni de Simone[a,b], **Richard B. Devereux**[a], **Marcello Chinali**[b], **Mary J. Roman**[a], **Thomas K. Welty**[c], **Elisa T. Lee**[d], and **Barbara V. Howard**[e]

a*Weill-Cornell Medical College, New York, New York, USA*

b*Federico II University Hospital, Naples, Italy*

c*Missouri Breaks Industry Research, Timber Lake, South Dakota*

d*University of Oklahoma, Oklahoma City, Oklahoma*

e*Medstar Research Institute, Washington, District of Columbia, USA*

Abstract

Objective—Metabolic abnormalities have been shown to predict 8-year incident arterial hypertension in individuals with optimal blood pressure. As echocardiographic left ventricular mass has also been reported to predict incident hypertension in individuals with baseline blood pressure of less than 140/90 mmHg, we determined whether left ventricular mass predicts 4-year incident hypertension also in individuals with initial optimal blood pressure (<120/80 mmHg), independent of metabolic factors influencing blood pressure.

Methods—We studied 777 of 3257 members of the American Indian population-based Strong Heart Study cohort with optimal blood pressure (34% men, 45% obese, and 35% diabetic), aged 57 ± 7 years, and without prevalent cardiovascular disease.

Results—Over 4 years, 159 individuals (20%, group H) developed hypertension (blood pressure ≥140/90 mmHg). They had a greater baseline BMI, waist girth, and blood pressure (112/69 vs. 109/68 mmHg, all $P<0.03$) than those remaining normotensive (group N), with similar lipid profile and renal function. At baseline, left ventricular mass was significantly greater in group H than in group N ($P<0.004$). The difference in left ventricular mass was confirmed after controlling for initial BMI, systolic blood pressure, homeostatic model assessment index, and diabetes. The probability of incident hypertension increased by 36% for each standard deviation of left ventricular mass index ($P=0.006$), independent of covariates. Participants with left ventricular mass of more than 159 g (75th percentile of distribution) had 2.5-fold (95% confidence interval, 1.4-3.6; $P<0.001$) higher adjusted risk of incident hypertension than those below this value.

Conclusion—Left ventricular mass predicts incident arterial hypertension in individuals with initially optimal blood pressure. This association is independent of body build, prevalent diabetes, and initial blood pressure.

Correspondence to Giovanni de Simone, MD, Department of Clinical and Experimental Medicine, Federico II University Hospital, via S. Pansini 5, building 1, 80131 Naples, Italy E-mail: simogi@unina.it.

There are no conflicts of interest.

Keywords

arterial load; diabetes; hypertension; hypertrophy; obesity; prevention; risk factors

Arterial hypertension is a complex, multifactorial hemodynamic condition driven by a variety of diseases and abnormalities of cardiovascular homeostasis, making it difficult to prevent its development and reduce its incidence by interventions on single aspects [1-4]. Metabolic risk factors, including obesity, dyslipidemia, and impaired glucose metabolism, can have vascular and hemodynamic effects that ultimately contribute to the development of arterial hypertension [5-7]. There is also evidence that unfavorable changes in these factors over time can potentiate the development of arterial hypertension [7]. Those associations, however, do not clarify why some but not other individuals exposed to these risk factors develop arterial hypertension.

Genetic factors, acting through different pathways, may contribute to the development of hypertension [1,8-10]. Several earlier studies suggested that higher left ventricular (LV) mass in normotensive individuals can predict subsequent hypertension [11-13], an observation that revitalized the concept that a more forceful cardiac pump could contribute to the development of high blood pressure (BP) in the presence of an arterial tree unable to either reduce peripheral resistance or increase conduit artery compliance or both [14]. Unfortunately, previous studies were conducted in population samples with normal or high-normal BP, but not optimal BP. Thus, they could not answer the question of whether the association between LV mass and incident hypertension was driven by initial BP in the range classified today as high-normal or prehypertensive, which may have already caused altered cardiac structure and function [15]. Whether LV mass is associated with the development of arterial hypertension in the presence of initial optimal BP is, therefore, unknown. Accordingly, the present study was designed to determine whether, in the presence of optimal baseline BP, a higher LV mass predicts incident arterial hypertension, independent of established cardiovascular risk factors.

Methods

Population

The Strong Heart Study (SHS) is a population-based longitudinal cohort study of cardiovascular risk factors and disease in American Indians from communities in Arizona, Southwestern Oklahoma and South and North Dakota, as extensively described [16-20].

During the second examination, in the years 1993-1996, participants also underwent a standard transthoracic echocardiographic study. Those with available information on body size and fat distribution, diabetes status, lipid profile, BP, and LV mass were first selected for the present analysis (n=3257). Participants with prevalent cardiovascular disease, including stroke, congestive heart failure, myocardial infarction, and other manifestations of coronary heart disease (assessed by coronary angiography or a combination of typical symptoms with positive treadmill tests or abnormal imaging stress test, or need for revascularization procedures), were excluded (n=394). Prevalent cardiovascular events were confirmed by the Strong Heart Study Mortality and Morbidity Committees, using specified criteria for causes of fatal and non-fatal cardiovascular events [21]. Diabetic and obese participants were included; however, similar to the criteria previously reported [7], only untreated participants with optimal baseline BP (<120/80 mmHg) [22-24] were included in the studied population sample. Thus, after exclusions, 777 participants with an optimal baseline BP at the time of the second SHS examination (261 men or 33.6%) and with a mean age of 57±7 years were considered in the present analysis.

Laboratory tests and classification of participants

BP measurements were accurately standardized in the SHS [25]. Briefly, BP was measured in the sitting position after a 5-min rest. After the first measurement, another two measurements were taken after raising the arm for 5 s and resting it on the table for another 25 s. The last two measurements were averaged to generate the reported BP value.

Fasting plasma glucose and lipid profile were measured by standard methods [18]. Diabetes was diagnosed by 1997 American Diabetes Association recommendations [26]. Homeostatic model assessment (HOMA) index was used to estimate insulin resistance [27]. Obesity was identified by BMI of at least 30 kg/m^2 based on 1998 National Institutes of Health (NIH) guidelines [28]. Waist circumference was used as an indicator of central adiposity according to 1998 NIH guidelines [28]. Glomerular filtration rate (GFR) was estimated by the simplified modification of diet in renal disease (MDRD) formula [29].

Echocardiographic measures

Measurements of interventricular and posterior wall thickness, and LV diastolic internal diameter, were taken using M-mode tracings or linear two-dimensional measures taken from the parasternal long axis view according to a well standardized method [30-32]. LV mass was calculated by a necropsy validated formula [33] and was normalized for body surface area and $height^{2.7}$ [34]. Left ventricular hypertrophy (LVH) was defined according to population-specific partition values (47.24 $g/m^{2.7}$), which have been prognostically validated [34].

Statistical analysis

Data were analyzed using SPSS 12.0 software (SPSS Inc, Chicago, Illinois, USA). Data are expressed as mean±one standard deviation (SD). Indicator variables were included in all multivariate analyses for the three field centers, Arizona, South/North Dakota, and Oklahoma. Incident hypertension was defined either as BP of at least 140 mmHg or 90 mmHg or both, or ongoing antihypertensive treatment at the time of the third SHS examination 46±9 months after the second examination. Descriptive statistics were obtained by one-factor analysis of variance (ANOVA) or χ^2 distribution. Changes over time of potential metabolic predictors of arterial hypertension were compared between the groups with or without incident hypertension by analysis of covariance (ANCOVA) for repeated measures, adjusting for age and sex. Adjusted means are displayed. The main potential confounders associated with follow-up hypertension were evaluated in binary logistic regression models. To evaluate whether LV mass index significantly added to the prediction of incident hypertension obtained with the main factors, a hierarchical model was generated by entering a primary block of main covariates, including age, sex, systolic blood pressure, BMI, diabetes, and HOMA index. LV mass index was, therefore, added to the primary model (secondary block). Likelihood functions were compared between the models without or with LV mass index [35]. The difference between the two likelihood functions has a χ^2 distribution, which, for this comparison, has one degree of freedom (i.e. one variable added to the model) [35].

Results

At the time of the second examination, 44.5% of the 777 participants were obese (50% of women and 33% of men) and diabetes was present in 34.7% of participants (38% of women and 28% of men, both $P<0.0001$).

By the time of the third SHS examination, incident arterial hypertension had developed in 159 participants (20% of men and 21% of women), 98 of whom (62%) were on medications. At baseline, participants developing hypertension during the follow-up were slightly more obese ($P<0.02$), had 3 mmHg higher average systolic BP with borderline higher diastolic BP; they

also had higher plasma glucose and HOMA index, and prevalence of diabetes, than participants maintaining normal BP (Table 1; all $P<0.0001$). No differences were found between groups in lipid profile, GFR, or heart rate. LVH was found in 62 participants (8%) and was 1.97-fold more prevalent among participants who developed hypertension than among those remaining normotensive [95% confidence interval (CI), 1.12-3.47; $P<0.03$].

Table 2 shows changes between the time of the second (baseline) and the third SHS examination in the metabolic profile of participants with or without hypertension detected at the time of the third SHS examination. Body weight increased in the entire population sample during follow-up. Adjusting for age and sex, individuals developing hypertension gained slightly more weight than those remaining normotensive ($P<0.03$). During follow-up, plasma glucose decreased significantly in the group developing hypertension ($P<0.002$), due to the effect of treatment of diabetes detected during the second examination, but remained higher than in those with persistent normal BP. No significant differences were detected in changes of lipid profile or GFR.

Baseline left ventricular geometry

At baseline, LV mass was higher in participants developing hypertension than in those remaining normotensive, in absolute terms and after normalization for body size (Table 3; all $P<0.0001$). Because the LV mass difference could be due to differences in clinical and metabolic factors (Tables 1 and 2), the comparison was repeated with adjustment for baseline systolic BP, BMI, HOMA index, and presence of diabetes. Table 3 also shows the adjusted means of baseline LV mass by different types of normalization for body size in participants with or without follow-up hypertension. Initial LV mass remained higher in participants developing arterial hypertension, irrespective of the method used to normalize for body size and after adjustment for main confounders.

Prediction of incident hypertension

After adjusting for sex, baseline BMI, systolic BP, HOMA index, and presence of diabetes or impaired fasting glucose, the probability of developing arterial hypertension over a 4-year follow-up increased by 39% for each 7.9 $g/m^{2.7}$ (corresponding to one SD in the whole population sample) of initial LV mass index [relative risk (RR), 1.39/7.9$g/m^{-2.7}$ (1.11-1.73, $P=0.004$)]. In addition to the LV mass index, higher initial systolic BP [RR, 1.07/mmHg (1.03-1.10; $P<0.0001$)] and presence of diabetes [RR, 2.59 (1.43-4.70; $P=0.002$)] were also independent predictors of incident hypertension, whereas no effect was found for HOMA index, BMI, and impaired fasting glucose.

Because of the significant effect of diabetes in the prediction of subsequent hypertension, diabetic and non-diabetic participants were also separately analyzed. LV mass index was significantly higher in the presence of diabetes (38.08±7.59 vs. 36.18±7.70 $g/m^{2.7}$; $P<0.02$, adjusted for systolic BP) and was confirmed as a predictor of incident hypertension in nondiabetic participants [RR, 1.84/7.9$g/m^{-2.7}$ (1.35-2.51; $P<0.0001$)] independent of the significant effect of systolic BP [RR, 1.06/mmHg (1.02-1.12; $P=0.009$)], without other significant contributions from sex, BMI, and HOMA index. In contrast, among diabetic participants, the only significant independent predictor of incident hypertension remained initial BP [RR, 1.07/mmHg (1.02-1.12; $P=0.004$)].

To examine whether the addition of LV mass index improved the prediction of incident hypertension in the whole population, we also used the χ^2 distribution to compare the likelihood functions of the model including all covariates but excluding LV mass index with the same model into which LV mass index was forced on the top of the primary variables. The -2log

likelihood function was 592 in the model without LV mass and 583 in the model including LV mass, a difference that was statistically significant ($P<0.005$).

Figure 1 shows the progressively higher likelihood of developing hypertension in progressively higher deciles of LV mass/height$^{2.7}$ obtained from the resulting functions from the logistic regression model. Participants in the highest decile of the distribution had a more than 30% likelihood of developing hypertension in the next 4 years. Participants with LV mass higher than the 75th percentile of the distribution in the SHS cohort (159 g) had a 2.5-foldhigher adjusted risk of developing arterial hypertension (1.42-3.60, $P<0.0005$) in the next 4 years than participants with LV mass 159 g or less, independent of the covariates used in the logistic regression model.

Discussion

The possibility that LV mass predicts future hypertension has been already reported in studies in relatively unselected populations [11-13] and in children with a family history of hypertension [36]. However, the entry criteria of those studies reflected old classifications of BP (i.e. <140/90 mmHg) [11,13] that included participants with high-normal and prehypertensive BP in the normotensive group [24,37]. According to recent guidelines, normal (optimal) BP values should be below 120/80 mmHg. Clinical evidence of optimal BP might be reasonably considered to confer a low risk of future high BP. In addition, in all the previous studies, LV mass was measured using only M-mode echocardiograms, a method that results in the exclusion of a large number of individuals due to body size, age, and other factors [38], whereas the combined M-mode and 2D approach used in the SHS allows measurement of LV mass in almost all participants, even if most are obese [38].

Thus, the present study is the first prospective analysis examining whether initial values of LV mass are associated with incident hypertension in a population-based cohort of individuals with initial optimal BP values and a broad range of body size and related metabolic abnormalities. Our analysis demonstrated that even when BP is optimal, the magnitude of LV mass measured by transthoracic echocardiography strongly predicts the probability of incident arterial hypertension.

Although BP is a pathophysiological continuum, from the practical standpoint, the evidence that LV mass is still a predictor of hypertension when the baseline variability of BP is constrained to the optimal range and, therefore, substantially limited (the coefficient of variability of systolic BP was as low as 7%) is relevant. In addition, unlike previous studies [11], our analysis also considered metabolic risk factors that others and we [5-7] have shown to be associated with the rise of BP over time, probably due to the progressive alteration of the arterial tree due to atherosclerosis. The conservative hierarchical approach we have used, giving LV mass a secondary value in the regression model compared with BP, body weight and abnormal glucose metabolism, confirmed that LV mass significantly adds to the prediction of 4-year incident hypertension obtained with the factors used as primary predictors. This result was also consistent in analyses with absolute values of LV mass or LV mass normalized for different measures of body size. Interestingly, the effect was substantially driven by the nondiabetic population with lower levels of LV mass, and therefore, with a more identifiable association than the subgroup with diabetes, which already presents with a more severe impairment of the cardiovascular system (33% of diabetic participants developed hypertension as compared with 14% of nondiabetic participants, independent of LV mass).

There are possible explanations of our findings. The SHS population has a high prevalence of central obesity [39], and masked hypertension is found more frequently in patients with central obesity [40]. In our study, arterial hypertension has been detected using office and not

ambulatory BP. Thus, the possibility that at least some participants with incident office arterial hypertension could have had masked hypertension [40] at the time of initial examination could not be ruled out. The prevalence of masked hypertension is reported to be about 10% in unselected populations [41,42]. This would imply that 70-80 participants in our study could have had masked hypertension. In addition, because of the variability of BP in day to day measures, there is also the possibility that the higher LV mass reflects a prolonged sustained exposure to higher BP, which cannot be captured by single office measurements, even if taken with a very standardized protocol. This has also been recently suggested by Kokkinos *et al*. [43] who reported that a change in BP from rest to five metabolic equivalents (i.e. a workload corresponding to most daily activities) is the strongest predictor of LV hypertrophy, whereas fitness protects from an excessive rise of BP during activity [44].

Although the above explanation is simple and plausible, this study also supports the possibility of reverse causation, not necessarily alternative to the possibility that some or many of our participants had masked hypertension. The concept that the power developed by the heart represents one of the mechanisms responsible for the increase in BP is supported by the evidence that hypertension can be predicted by the increase in BP during exercise. This exercise-induced increase in BP is in turn associated with a high LV mass [45], a finding that parallels the detection of masked hypertension by ambulatory monitoring during daily activities, a time when the blood supply requirements are higher than during the resting conditions at the office visit [46,47]. An equilibrium among pump force, circulating flow, conduit artery compliance and elasticity and peripheral resistance to blood flow is a requisite for the circulatory system to maintain fluid pressure [48-50]. Thus, the development of arterial hypertension requires a convergence of alterations of different factors, including cardiovascular musculature, heart strength and magnitude of circulating volume, which result in BP augmentation when the elasticity of conduit arteries and peripheral resistance are impaired by the adverse effect of atherogenic risk factors, all elements that can be found in our analyses [7].

In our previous study [7], abdominal obesity and its progression were strongly associated with 8-year incident arterial hypertension, despite the relatively small range of variability of these parameters in this population, consistent with the evidence that obesity and the associated neurohormonal patterns are well documented predictors of future hypertension in epidemiological and clinical studies [51,52]. In the present shorter follow-up, obesity and a higher BMI were also associated with incident hypertension in univariate analysis, but their effect in the model was obscured by other cofactors, including LV mass index, suggesting that an increased LV mass might integrate at least a part of the effect of alteration of body size on incident hypertension. This finding is also in line with previous evidence that genes common to LV mass and body weight significantly influence their covariance and that as much as 90% of the LV mass-body weight relation might be due to common genes [53].

In conclusion, we provide evidence that LV mass is a predictor of 4-year incident arterial hypertension in a population-based sample with high prevalence of obesity but initial optimal BP. This prediction is independent of metabolic and anthropometric factors already demonstrated to be associated with incident hypertension.

The possibility to refine the identification of a phenotype at high risk of arterial hypertension, by pooling metabolic information with the measure of LV mass, increases the chance to target individuals that might benefit from preventive treatment, as already proposed for high-normal BP values. Further research is needed to quantify the possible impact of masked hypertension on the association between LV mass and incident office hypertension and clarify their cause-effect relationship.

Acknowledgements

The authors wish to thank the Indian Health Service, the Strong Heart Study participants, the participating tribal communities and the Strong Heart Study Center coordinators for their help in the realization of this project.

Views expressed in this study are those of the authors and do not necessarily reflect those of the Indian Health Service.

This work has been supported by grants HL41642, HL41652, HL41654, HL65521 and M10RR0047-34 (GCRC) from the National Institutes of Health, Bethesda, Maryland, USA.

Abbreviations

BMI, Body mass index; GFR, Glomerular filtration rate; HOMA, Homeostatic model assessment; LVH, Left ventricular hypertrophy; MDRD, Modification of diet in renal disease; SHS, Strong Heart Study.

References

1. Hamilton M, Pickering GW, Roberts JA, Sowry GS. The aetiology of essential hypertension. 4. The role of inheritance. Clin Sci (Lond) 1954;13:273–304. [PubMed: 13161192]
2. Pickering GW, Roberts JA, Sowry GS. The aetiology of essential hypertension. 3. The effect of correcting for arm circumference on the growth rate of arterial pressure with age. Clin Sci (Lond) 1954;13:267–271. [PubMed: 13161191]
3. Hamilton M, Pickering GW, Roberts JA, Sowry GS. The aetiology of essential hypertension. II. Scores for arterial blood pressures adjusted for differences in age and sex. Clin Sci (Lond) 1954;13:37–49. [PubMed: 13141422]
4. Hamilton M, Pickering GW, Roberts JA, Sowry GS. The aetiology of essential hypertension. I. The arterial pressure in the general population. Clin Sci (Lond) 1954;13:11–35. [PubMed: 13141421]
5. Dyer AR, Liu K, Walsh M, Kiefe C, Jacobs DR Jr, Bild DE. Ten-year incidence of elevated blood pressure and its predictors: the CARDIA study. Coronary Artery Risk Development in (Young) Adults. J Hum Hypertens 1999;13:13–21. [PubMed: 9928747]
6. Borghi C, Veronesi M, Bacchelli S, Esposti DD, Cosentino E, Ambrosioni E. Serum cholesterol levels, blood pressure response to stress and incidence of stable hypertension in young subjects with high normal blood pressure. J Hypertens 2004;22:265–272. [PubMed: 15076183]
7. de Simone G, Devereux RB, Chinali M, Roman MJ, Best LG, Welty TK, et al. Risk factors for arterial hypertension in adults with initial optimal blood pressure: the Strong Heart Study. Hypertension 2006;47:162–167. [PubMed: 16380527]
8. Hunt SC, Hasstedt SJ, Kuida H, Stults BM, Hopkins PN, Williams RR. Genetic heritability and common environmental components of resting and stressed blood pressures, lipids, and body mass index in Utah pedigrees and twins. Am J Epidemiol 1989;129:625–638. [PubMed: 2916556]
9. Snieder H, Hayward CS, Perks U, Kelly RP, Kelly PJ, Spector TD. Heritability of central systolic pressure augmentation: a twin study. Hypertension 2000;35:574–579. [PubMed: 10679500]
10. Snieder H, Harshfield GA, Treiber FA. Heritability of blood pressure and hemodynamics in African- and European-American youth. Hypertension 2003;41:1196–1201. [PubMed: 12719445]
11. de Simone G, Devereux RB, Roman MJ, Schlussel Y, Alderman MH, Laragh JH. Echocardiographic left ventricular mass and electrolyte intake predict arterial hypertension. Ann Intern Med 1991;114:202–209. [PubMed: 1984744]
12. Iso H, Kiyama M, Doi M, Nakanishi N, Kitamura A, Naito Y, et al. Left ventricular mass and subsequent blood pressure changes among middle-aged men in rural and urban Japanese populations. Circulation 1994;89:1717–1724. [PubMed: 8149537]
13. Post WS, Larson MG, Levy D. Impact of left ventricular structure on the incidence of hypertension. The Framingham Heart Study. Circulation 1994;90:179–185. [PubMed: 8025994]
14. Dustan HP, Tarazi RC. Cardiogenic hypertension. Annu Rev Med 2006;29:485–493. [PubMed: 348044]

15. Drukteinis JS, Roman MJ, Fabsitz RR, Lee ET, Best LG, Russell M, Devereux RB. Cardiac and systemic hemodynamic characteristics of hypertension and prehypertension in adolescents and young adults: the Strong Heart Study. Circulation 2007;115:221–227. [PubMed: 17210838]
16. Lee ET, Fabsitz R, Cowan LD, Le NA, Oopik AJ, Cucchiara AJ, et al. The Strong Heart Study: a study of cardiovascular disease in American Indians: design and methods. Am J Epidemiol 1990;136:1141–1155. [PubMed: 2260546]
17. Howard BV, Lee ET, Yeh JL, Go O, Fabsitz RR, Devereux RB, Welty TK. Hypertension in adult American Indians. The Strong Heart Study. Hypertension 1996;28:256–264. [PubMed: 8707391]
18. Welty TK, Lee ET, Yeh J, Cowan LD, Go O, Fabsitz RR, et al. Cardiovascular disease risk factors among American Indians. The Strong Heart Study. Am J Epidemiol 1995;142:269–287. [PubMed: 7631631]
19. Lee ET, Cowan LD, Welty TK, Sievers M, Howard WJ, Oopik A, et al. All-cause mortality and cardiovascular disease mortality in three American Indian populations, aged 45-74 years, 1984-1988. The Strong Heart Study. Am J Epidemiol 1998;147:995–1008. [PubMed: 9620042]
20. Devereux RB, Roman MJ, Paranicas M, O'Grady MJ, Lee ET, Welty TK, et al. Impact of diabetes on cardiac structure and function: the strong heart study. Circulation 2000;101:2271–2276. [PubMed: 10811594]
21. Howard BV, Lee ET, Cowan LD, Devereux RB, Galloway JM, Go OT, et al. Rising tide of cardiovascular disease in American Indians. The Strong Heart Study. Circulation 1999;99:2389–2395. [PubMed: 10318659]
22. Joint National Committee on Detection EaToHBP. The sixth report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413–2446. [PubMed: 9385294]
23. Lenfant C, Chobanian AV, Jones DW, Roccella EJ. Seventh report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7): resetting the hypertension sails. Hypertension 2003;41:1178–1179. [PubMed: 12756222]
24. Practice Guidelines Writing Committee. Practice guidelines for primary care physicians: 2003 ESH/ESC hypertension guidelines. J Hypertens 2003;21:1779–1786. [PubMed: 14508180]
25. Strong Heart Study. SHS operation manual. Phase 2. Center for American Indian Health Research, College of Public Health, University of Oklahoma Health Sciences; Oklahoma: 2007. http://strongheart.ouhsc.edu/manual/PhaseII/Physical%20examination.pdf
26. American Diabetes Association. American Diabetes Association: clinical practice recommendations 1997. Diabetes Care 1997;20:S1–S70. [PubMed: 9028710]
27. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412–419. [PubMed: 3899825]
28. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Obes Res 1998;6(Suppl 2):51S–209S. [PubMed: 9813653]
29. Stevens LA, Coresh J, Greene T, Levey AS. Assessing kidney function: measured and estimated glomerular filtration rate. N Engl J Med 2006;354:2473–2483. [PubMed: 16760447]
30. Sahn DJ, DeMaria A, Kisslo J, Weyman A. Recommendations regarding quantitation in M-mode echocardiography: results of a survey of echocardiographic measurements. Circulation 1978;58:1072–1083. [PubMed: 709763]
31. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux RB, Feigenbaum H, et al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am Soc Echocardiogr 1989;2:358–367. [PubMed: 2698218]
32. Palmieri V, Dahlof B, DeQuattro V, Sharpe N, Bella JN, de Simone G, et al. Reliability of echocardiographic assessment of left ventricular structure and function: the PRESERVE study. Prospective Randomized Study Evaluating Regression of Ventricular Enlargement. J Am Coll Cardiol 1999;34:1625–1632. [PubMed: 10551715]see comments

33. Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, Reichek N. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. Am J Cardiol 1986;57:450–458. [PubMed: 2936235]
34. de Simone G, Kizer JR, Chinali M, Roman MJ, Bella JN, Best LG, et al. Normalization for body size and population-attributable risk of left ventricular hypertrophy: The Strong Heart Study. Am J Hypertens 2005;18:191–196. [PubMed: 15752946]
35. Collett, D. Modelling survival data in medical research. Chapman & Hill; London: 1996.
36. Cook BB, Treiber FA, Mensah G, Jindal M, Davis HC, Kapuku GK. Family history of hypertension and left ventricular mass in youth: possible mediating parameters. Am J Hypertens 2001;14:351–356. [PubMed: 11336181]
37. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, et al. The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA 2003;289:2560–2572. [PubMed: 12748199]
38. Devereux RB, Roman MJ, Liu JE, Lee ET, Wang W, Fabsitz RR, et al. An appraisal of echocardiography as an epidemiological tool. The Strong Heart Study. Ann Epidemiol 2003;13:238–244. [PubMed: 12684189]
39. Gray RS, Fabsitz RR, Cowan LD, Lee ET, Howard BV, Savage PJ. Risk factor clustering in the insulin resistance syndrome. The Strong Heart Study. Am J Epidemiol 1998;148:869–878. [PubMed: 9801017]
40. Pickering TG, Davidson K, Gerin W, Schwartz JE. Masked hypertension. Hypertension 2002;40:795–796. [PubMed: 12468559]
41. Papadopoulos DP, Makris TK. Masked hypertension definition, impact, outcomes: a critical review. J Clin Hypertens (Greenwich) 2007;9:956–963. [PubMed: 18046102]
42. Pickering TG, Eguchi K, Kario K. Masked hypertension: a review. Hypertens Res 2007;30:479–488. [PubMed: 17664850]
43. Kokkinos P, Pittaras A, Narayan P, Faselis C, Singh S, Manolis A. Exercise capacity and blood pressure associations with left ventricular mass in prehypertensive individuals. Hypertension 2007;49:55–61. [PubMed: 17088448]
44. Kokkinos P, Pittaras A, Manolis A, Panagiotakos D, Narayan P, Manjoros D, et al. Exercise capacity and 24-h blood pressure in prehypertensive men and women. Am J Hypertens 2006;19:251–258. [PubMed: 16500509]
45. Wilson NV, Meyer BM. Early prediction of hypertension using exercise blood pressure. Prev Med 1981;10:62–68. [PubMed: 7232344]
46. Mahoney LT, Schieken RM, Clarke WR, Lauer RM. Left ventricular mass and exercise responses predict future blood pressure. The Muscatine Study. Hypertension 1988;12:206–213. [PubMed: 3410529]
47. Miyai N, Arita M, Miyashita K, Morioka I, Shiraishi T, Nishio I. Blood pressure response to heart rate during exercise test and risk of future hypertension. Hypertension 2002;39:761–766. [PubMed: 11897759]
48. Westerhof N, Sipkema P, Vis MA. How cardiac contraction affects the coronary vasculature. Adv Exp Med Biol 1997;430:111–121. [PubMed: 9330723]
49. Stergiopulos N, Westerhof BE, Westerhof N. Total arterial inertance as the fourth element of the windkessel model. Am J Physiol 1999;276:H81–H88. [PubMed: 9887020]
50. Stergiopulos N, Westerhof N. Role of total arterial compliance and peripheral resistance in the determination of systolic and diastolic aortic pressure. Pathol Biol (Paris) 1999;47:641–647. [PubMed: 10472075]
51. Chuang SY, Chou P, Hsu PF, Cheng HM, Tsai ST, Lin IF, Chen CH. Presence and progression of abdominal obesity are predictors of future high blood pressure and hypertension. Am J Hypertens 2006;19:788–795. [PubMed: 16876676]
52. Shintani M, Ikegami H, Fujisawa T, Kawaguchi Y, Ohishi M, Katsuya T, et al. Leptin gene polymorphism is associated with hypertension independent of obesity. J Clin Endocrinol Metab 2002;87:2909–2912. [PubMed: 12050272]

53. Verhaaren HA, Schieken RM, Mosteller M, Hewitt JK, Eaves LJ, Nance WE. Bivariate genetic analysis of left ventricular mass and weight in pubertal twins (the Medical College of Virginia twin study). Am J Cardiol 1991;68:661–668. [PubMed: 1877484]

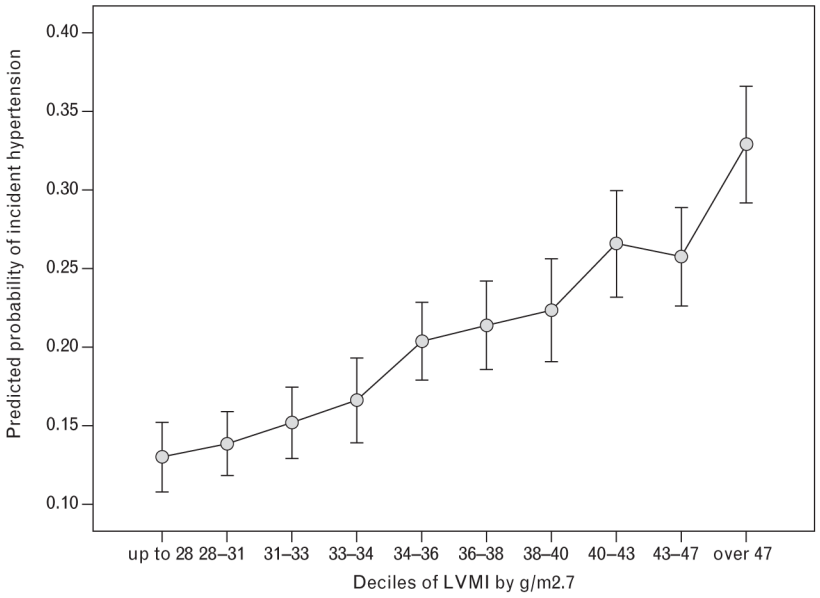

Fig. 1.

Adjusted probability of 4-year incident hypertension in relation to initial deciles of left ventricular mass index. LVMI, left ventricular mass index.

Table 1

Characteristics of participants with optimal blood pressure

Characteristics	Remaining normotensive (*n*=618)	Developing hypertension (*n*=159)	*P* value
Age (years)	57.0±6.7	57.3±7.0	NS
Men/women	412/206	104/55	NS
BMI (kg/m^2)	29.5±5.9	30.7±6.0	≤0.02
Waist circumference (cm)	102.3±14.9	105.3±13.5	≤0.03
Systolic BP (mmHg)	108.8±8.0	112.0±7.1	≤0.0001
Diastolic BP (mmHg)	67.8±6.9	68.9±6.2	NS
Heart rate (bpm)	71.3±10.6	72.9±10.2	NS
Fasting glucose (mg/dl)	135.4±73.1	177.0±91.6	≤0.0001
Diabetes *n* (%)	180 (29)	88 (55)	≤0.0001
HOMA index	6.7±9.7	9.7±10.8	≤0.0001
Total cholesterol (mg/dl)	191.0±37.7	189.7±37.2	NS
Triglycerydes (mg/dl)	148.9±108.4	145.7±89.2	NS
HDL cholesetrol (mg/dl)	40.9±12.3	41.1±13.2	NS
LDL cholesterol (mg/dl)	121.6±33.4	119.8±32.0	NS
Non-HDL-cholesterol (mg/dl)	149.9±37.9	148.8±38.8	NS
GFR (ml/min)	86.4±29.5	86.2±28.9	NS

Comparison has been done between those remaining normotensive and those exhibiting arterial hypertension at the time of third Strong Heart Study examination. BMI, body mass index; BP, blood pressure; bpm, beats per minute; GFR, glomerular filtration rate; HDL, high-density lipoprotein; HOMA, homeostatic model assessment; LDL, low-density lipoprotein; NS, not significant.

J Hypertens. Author manuscript; available in PMC 2008 October 31.

Table 2

Changes of anthropometric measures and metabolic risk factors during 4 year follow-up in subjects developing hypertension or remaining normotensive

	Remaining normotensive (*n*=618)		Developing hypertension (*n*=159)		
	Second examination	Third examination	Second examination	Third examination	*P* value
Body weight (kg)	80.2±17.0	83.4±17.6	80.4±17.5	83.8±18.0	≤0.03
Waist girth (cm)	102.3±15.0	105.4±15.2	101.8±13.5	105.5±14.8	NS
Plasma glucose (mg/dl)	134.8±73.0	130.1±63.6	174.2±90.8	150.8±72.1	<0.002
HDL cholesterol (mg/dl)	40.9±12.3	41.1±12.8	43.0±12.5	44.4±15.1	NS
LDL cholesterol (mg/dl)	121.9±33.7	120.0±32.3	120.7±32.5	118.5±34.2	NS
Total cholesterol (mg/dl)	191.6±37.8	189.1±38.3	191.3±35.5	190.6±40.9	NS
Plasma triglycerydes (mg/dl)	149.8±109.7	141.0±85.4	141.2±74.4	139.6±89.1	NS
GFR (ml/min)	86.2±29.3	86.6±28.3	89.5±28.3	87.6±30.1	NS

P values refer to the difference between the interaction effect of time and grouping characteristics. GFR, glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NS, not significant.

Table 3

Baseline left ventricular mass in participants remaining normotensive or developing hypertension

	Remaining normotensive (*n*=618)		Developing hypertension (*n*=159)		
	Unadjusted	**Adjusted**	**Unadjusted***	**Adjusted**	***P* value**
LV mass (g)	138.0±28.4	138.6±27.6	148.4±33.6	147.8±28.2	<0.009
LV mass index (g/m^2 BSA)	74.4±12.7	74.4±13.3	78.5±15.5	79.0±13.6	<0.007
LV mass index (g/m$^{2.7}$ height)	36.1±7.2	36.3±6.8	39.0±9.0	38.5±6.9	<0.008

Mean values are shown as raw values and after adjusting for confounding risk factors (see also text). *P* values are adjusted. LV, left ventricular; BSA, body surface area.

* All *P*<0.0001.