Impact of abdominal obesity and ambulatory blood pressure in the diagnosis of left ventricular hypertrophy in never treated hypertensives

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ABSTRACT

Background and objectives: The principal objective was to assess the prevalence of left ventricular hypertrophy (LVH) in hypertensive, never treated patients, depending on adjustment for body surface or height. Secondary objectives were to determine geometric alterations of the left ventricle and to analyze the interdependence of hypertension and obesity to induce LVH.

Patients and methods: Cross-sectional study that included 750 patients (387 men) aged 47 (13, SD) years who underwent ambulatory blood pressure (ABPM) monitoring and echocardiography.

Results: The prevalence of LVH was 40.4% (303 patients), adjusted for body surface area (BSA, LVH BSA), and 61.7% (463 patients), adjusted for height 2.7 (LVH height 2.7). In a multivariate logistic analysis, systolic BP 24h, gender and presence of elevated microalbuminuria were associated with both LVH BSA and LVH height 2.7. Increased waist circumference was the strongest independent predictor of LVH height 2.7, but was not associated with LVH BSA. We found a significant interaction between abdominal obesity and systolic BP 24h in LVH height 2.7. Concentric remodelling seems to be the most prevalent alteration of left ventricular geometry in early stages of hypertension (37.5%).

Conclusions: The impact of obesity as predictor of LVH in never treated hypertensives is present only when left ventricular mass (LVM) is indexed to height 2.7. Obesity interacts with systolic BP 24h in an additive but not merely synergistic manner. Systolic BP 24h is the strongest determinant of LVH when indexed for BSA.

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Impacto de la obesidad abdominal y la presión arterial ambulatoria en el diagnóstico de hipertrofia ventricular izquierda en hipertensos no tratados

RESUMEN

Fundamento y objetivos: El objetivo principal es determinar la prevalencia de la hipertrofia ventricular izquierda (HV1) en hipertensos no tratados previamente según ajuste por superficie corporal o talla. Los objetivos secundarios son establecer las alteraciones de la geometría ventricular y analizar la interdependencia entre hipertensión y obesidad para inducir HV1.

Pacientes y método: Estudio transversal en 750 sujetos (387 varones) con una edad media de 47 años (DE 13) a los que se les practicó monitorización ambulatoria de la presión arterial y ecocardiografía.

Resultados: La prevalencia de HV1 fue del 40.4% (303 pacientes) ajustando por superficie corporal (HV1SC), y del 61.7% (463 pacientes) ajustando por talla 2.7 (HV1talla2.7). En un análisis logístico multivariante, la PA sistólica de 24 h, el sexo y la presencia de microalbuminuria elevada se asociaron...
Introduction

Left ventricular hypertrophy (LVH) may be detected early in uncontrolled hypertension by echocardiography and is recognized as an independent clinical risk factor for cardiac failure, sudden death, myocardial infarction and stroke. Furthermore, LVH completely fulfills the criteria to be considered an adequate surrogate end-point for morbid events in hypertension.

The definition for echocardiographic LVH, however, is far from homogeneous. A recent review including 39 randomized trials on regression of LVH in hypertensive patients found up to 19 different echocardiographic criteria for defining LVH, which leads to a significant distortion of the association between LVH and cardiovascular disease. This high variability reflects the combination of several partition values for three main sources of the physiologic determination of LV mass (LVM): gender, obesity and lean body mass. The vast majority of studies adjust LVM for body surface area (BSA), and since 2003 the European Society of Hypertension has defined the presence or absence of LVH according to a normalization using BSA. Notwithstanding, in recent years allometric height adjustment of LVM has become increasingly recognized as a useful tool in estimating cardiovascular risk of hypertensive patients more accurately, with separate cut-off values for men and for women.

The principal objective of our study was to assess the prevalence of LVH in hypertensive, never treated patients, depending on adjustment for body surface or height. Secondary objectives were to determine geometric alterations of the left ventricle and to analyze the interdependence of the two principal causing factors, hypertension and obesity, to induce LVH.

Patients and methods

Selection of study participants and design

This cross-sectional study included subjects, all Caucasians, recruited consecutively from the hypertension outpatient clinic of the Hospital General of Sagunto (Sagunto, Spain) from 1st January 2005 to 31st October 2009. Patients, referred from Primary Care, were selected if they had any of the following Blood Pressure (BP) values: (a) office BP ≥140 mmHg for systolic and/or ≥90 mmHg for diastolic BP in each of three visits within a month’s time, or BP values ≥130 mmHg for systolic or ≥80 mmHg for diastolic recorded during a 24-h ambulatory BP monitoring (ABPM) during the same period (b) echocardiographic assessment of LVM using an acceptable visualization of interfaces, and (c) no previous antihypertensive therapy. Patients with secondary hypertension, nephropathy, diabetes mellitus and urinary tract infection, or previous vascular, cardiac or cerebral disease were excluded. The study was approved by the Ethical Committee of the Sagunto Hospital, and all participants gave informed written consent.

At the beginning, and when appropriate, a clinical work-up was carried out in order to exclude secondary hypertension. After evaluation, patients were placed in usual care treatment. This included a non-pharmacological treatment consisting of moderate salt restriction and a low-calorie diet, if overweight. If necessary, treatment with antihypertensive drugs was started.

Procedures

BP was measured using a mercury sphygmomanometer following the recommendations of the British Hypertension Society and with a validated Omron HEM 705-CP monitor after 2009. Systolic BP (SBP) and diastolic BP (DBP) were the average of 3 readings measured at 5-min intervals. Blood samples were obtained in the morning after a minimum of 8 h of fasting. Serum biochemical profiles were measured using a multiple-channel autoanalyzer. The glomerular filtration rate was estimated (EGFR) by the MDRD abbreviated formula. Urinary albumin excretion (UAE) was expressed as the ratio of albumin (mg) to creatinine excretion (g). For each patient, the UAE was considered as the mean value obtained in the two separate samples. The cut-off values for the presence of microalbuminuria were ≥22 mg/g in men and ≥31 mg/g in women. Obesity was defined according to the waist circumference (102 cm in men, 88 cm in women) on the basis of the Guidelines for the Management of Arterial Hypertension and the Adult Treatment Panel III criteria. The definition of metabolic syndrome (MS) followed also these criteria.

Ambulatory blood pressure monitoring (ABPM)

A portable, non-invasive SpaceLabs 90207 recorder (SpaceLabs, Redmond, WA) was used to perform the 24-h ABPM. The BP readings were performed automatically at 15-min intervals during the day and at 20-min intervals during night-time resting. The time periods were standardized according to the time at which the patients rose and retired. Systolic readings ≥260 mmHg or ≤70 mmHg, diastolic readings ≥150 mmHg or ≤40 mmHg, and pulse pressure readings ≥150 mmHg or ≤20 mmHg were automatically discarded.

Echocardiography

Echocardiography was carried out using commercially available instruments (Hewlett Packard Sonos 1000). The recommendations of the American Society of Echocardiography for image orientation were followed. M-mode echocardiograms with two-dimensional guidance were recorded with the patients in the left lateral decubitus position after a rest of at least 10 min. Standard projections were used (longitudinal, parasternal, 2 and 4 chamber apical, and subcostal), directing the M-mode cursor through the centre of the two-dimensional parasternal short-axis image immediately distal to the tips of the mitral valve leaflets. It was mandatory to align the M-mode cursor perpendicular to the long axis of the ventricle to obtain a clear definition of endocardial and epicardial interfaces. Wall thicknesses to calculate LVM were measured at end diastole on at least three cardiac cycles. Only frames with optimal images and showing simultaneously the interventricular septum, left ventricular internal diameter and posterior wall, were employed. All echocardiographic studies were recorded and read by two expert echocardiographers. The
recordings were always read by the same observers at the same centre. The interobserver coefficients of variation of the measurements were around 2% for left ventricular end-diastolic diameter, and between 4 and 6% for septal and posterior left ventricular wall thickness, respectively. Left ventricular mass (LVM) was calculated according to a necropsy-validated formula and normalized in two ways: (a) with respect to body surface area (BSA) in m², as LVMI_{BSA}; and (b) normalized for height^{2.7}, as LVMI_{height}. Left ventricular hypertrophy (LVH) was defined according to the most widely used criteria at the time of the study design and according to the Guidelines for the Management of Arterial Hypertension of theESH, that is, in the first case as LVMI_{BSA} when LVMI_{BSA} ≥ 125 g/m² in men and LVMI_{BSA} ≥ 110 g/m² in women, and in the second case as LVH_{height} when LVMI_{height} ≥ 51 g/m² for men and LVMI_{height} ≥ 47 g/m² for women, according to Cuspidi et al. Relative wall thickness (RWT) was calculated by the formula: septal wall thickness plus posterior wall thickness divided by LV diastolic diameter. The reference cut point value used for increased relative wall thickness was 0.42. \(^\text{12}\)

**Statistical analysis**

The results are shown as average ± standard deviation (SD) for continuous variables normally distributed, as the median and interquartile interval (IQI) for variables with skewed distribution, and as a percentage for categorical variables. Differences in parameters of interest between groups were sought by \( T \) test, U Mann–Whitney test and Chi-square test for categorical variables. Differences in parameters within each group were checked by the paired samples \( T \)-test, Wilcoxon test and McNemar test for categorical variables. To study the strength of the linear association between variables, the Pearson correlation coefficient was used. Then, a linear multiple regression model was performed with LVMI as the dependent variable. For selecting independent variables, the backwards stepwise method was used. Logistic regression analysis was used to assess the prognostic factors of LVH and to test the effect of interactions between variables. Statistical significance was assumed if \( p < 0.05 \) (two-tailed). SSPS 17 was used to perform the analysis.

**Results**

**General characteristics of patients**

Of the 833 patients initially evaluated, 83 were excluded due to low quality echocardiography or ABPM. These patients did not differ in their clinical characteristics from the patients who were recruited (data not shown). The general characteristics of the remaining 750 patients are shown in Table 1.

The sample, 387 males (52%), had a median age of 47 (13 SD) years, office BP was SBP 141 (15) mmHg and DBP 85 (10) mmHg, and in ABPM SBP_{24h} was 133 (12) mmHg and DBP_{24h}, 84 (10) mmHg. Of these, 119 (16%) had microalbuminuria. 221 (30% of the total) had metabolic syndrome. Thus, this group is representative of a middle-aged population with mild hypertension and without previous antihypertensive pharmacological treatment.

**Definition and prevalence of LVH**

Prevalence of LVH was lower when LVM was normalized by BSA (LVMI_{BSA}), 303 of 750 (40.4%), than it was by height^{2.7} (LVH_{height}), 463 of 750 patients (61.7%). In both cases, the prevalence was significantly higher in men than in women (LVMI_{BSA}: 59.7% vs. 46.1%, \( \chi^2 13.5; p = 0.0001 \), LVH_{height}: 56.4% vs. 43.9%, \( \chi^2 11.0; p = 0.001 \), respectively).

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Characteristics of the patients included in the study.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>750</td>
</tr>
<tr>
<td>Gender (male), n (%)</td>
<td>387 (52)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47 (13)</td>
</tr>
<tr>
<td>LVMI_{BSA} (g/m²)^a</td>
<td>115 (94–132)</td>
</tr>
<tr>
<td>LVMI_{height} (g/m²)^a</td>
<td>55 (45–63)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>93 (18)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>79 (17)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>29 (5)</td>
</tr>
<tr>
<td>Metabolic syndrome, n (%)</td>
<td>221 (30)</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>141 (15)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>85 (10)</td>
</tr>
<tr>
<td>SBP_{24h} (mmHg)</td>
<td>133 (12)</td>
</tr>
<tr>
<td>DBP_{24h} (mmHg)</td>
<td>84 (10)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>76 (13)</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)^a</td>
<td>100 (90–104)</td>
</tr>
<tr>
<td>Creatinine (mg/dl)^a</td>
<td>0.9 (0.8–1.0)</td>
</tr>
<tr>
<td>ECFR (ml/min/1.73 m²)^a</td>
<td>89 (76–98)</td>
</tr>
<tr>
<td>Uric acid (mg/dl)</td>
<td>5.4 (1.5)</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>203 (38)</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dl)</td>
<td>55 (44–65)</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dl)</td>
<td>122 (35)</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)^a</td>
<td>124 (73–147)</td>
</tr>
<tr>
<td>Urinary albumin excretion (µg/g Cr)^a</td>
<td>8 (5–16)</td>
</tr>
<tr>
<td>Microalbuminurias, n (%)</td>
<td>119 (16)</td>
</tr>
<tr>
<td>Smoking, n (%)</td>
<td>184 (25)</td>
</tr>
</tbody>
</table>

Data presented as average (standard deviation, SD). \(^a\) Data presented as median (interquartile interval, IQI): LVMI_{BSA}, left ventricular mass index adjusted for body surface area; LVH_{height}, left ventricular mass index adjusted for height^{2.7}; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ECFR, estimated glomerular filtration rate; UAE, urinary albumin excretion; HDL-cholesterol, high density lipoprotein cholesterol; LDL-cholesterol, low density lipoprotein cholesterol.

**Characteristics of patients with LVH**

In both categories of adjustment, patients with LVH were older when compared to patients without LVH, they presented higher office and ambulatory BP, had a higher prevalence of microalbuminuria, greater waist circumference, higher cardiovascular risk, lower heart rate and lower HDL-cholesterol (Table 2). Total cholesterol and LDL-cholesterol were significantly higher only in LVH_{height}.

Of the 303 patients who had LVMI_{BSA}, 301 also had LVH_{height}, 162 patients had LVH_{height} when normalizing only by height^{2.7}, not by BSA. Table 3 shows that patients in the last group were predominantly women, and that they presented higher waist circumference, lower systolic and diastolic BP, lower prevalence of microalbuminuria, and higher heart rate.

**Factors correlated to LVMI**

All BP measurements were significantly correlated to LVMI (data not shown), whatever the system of LVH classification used, but systolic ambulatory BP (SBP_{24h}) showed the strongest association with LVMI_{BSA} (\( r = 0.417 \)) and LVH_{height} (\( r = 0.425 \)). The waist circumference also correlated with LVMI_{BSA} (\( r = 0.276 \)), and LVH_{height} (\( r = 0.392 \)). UAE, age, glucose and EGFR were also related to LVMI, but the relation was weaker. In stepwise linear multiple regression, only SBP_{24h}, and UAE were factors associated with LVMI_{BSA}, correcting for age and gender. The factors associated with LVH_{height}, after correcting for age (gender was not significant), were SBP_{24h} and UAE again. This time, however, waist circumference emerged as strongly significant (Table 4A and B).

**Variables related to LVH adjusted by BSA**

In multivariate logistic regression analysis using LVH_{BSA} as the dependent variable (Table 5A), only male gender,
Table 2
Characteristics of patients with and without LVH.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adjustment for BSA</th>
<th>p</th>
<th>Adjustment for height$^{2,7}$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVM$_{BSA}$ (g/m$^2$)$^a$</td>
<td>n = 303/40.4%</td>
<td>n = 447/59.6%</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>LVM$_{Bheight}$(g/m$^2$)$^a$</td>
<td>66 (60–73)</td>
<td>46 (41–52)</td>
<td>0.05</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age, years</td>
<td>48 (12)</td>
<td>46 (12)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Gender male, n (%)</td>
<td>181 (59.7)</td>
<td>206 (46.1)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>146 (18)</td>
<td>138 (15)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>88 (12)</td>
<td>82 (9)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>SBP$_{ma}$ (mmHg)</td>
<td>138 (14)</td>
<td>130 (12)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>SBP$_{da}$ (mmHg)</td>
<td>87 (11)</td>
<td>82 (9)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Microalbuminuria (n, %)</td>
<td>69 (23)</td>
<td>50 (11)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.8 (13)</td>
<td>91.4 (13)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>CV-risk (Framingham-score$^a$)</td>
<td>3 (1–6)</td>
<td>2 (1–5)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>74 (12)</td>
<td>78 (14)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>HDL-C (mg/dl)$^a$</td>
<td>51 (42–62)</td>
<td>56 (45–66)</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>204 (38)</td>
<td>203 (38)</td>
<td>0.73</td>
<td>0.030</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>124 (35)</td>
<td>121 (35)</td>
<td>0.20</td>
<td>0.002</td>
</tr>
<tr>
<td>Glucose (mg/dl)</td>
<td>97 (91–106)</td>
<td>96 (82–103)</td>
<td>0.20</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Data are presented as average (standard deviation, SD).

Table 3
Differences between patients with LVH depending on adjustment.

<table>
<thead>
<tr>
<th>LVM$_{BSA}$</th>
<th>LVM$_{Bheight}$</th>
<th>Only LVM$_{Bheight}$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 301</td>
<td>n = 162</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVM$_{BSA}$ (g/m$^2$)$^a$</td>
<td>138 (127–153)</td>
<td>108 (100–118)</td>
<td>0.0001</td>
</tr>
<tr>
<td>LVM$_{Bheight}$ (g/m$^2$)$^a$</td>
<td>66 (60–74)</td>
<td>54 (51–57)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Age, years</td>
<td>48 (12)</td>
<td>50 (11)</td>
<td>ns</td>
</tr>
<tr>
<td>Gender (male), n (%)</td>
<td>180 (59.8)</td>
<td>81 (50.0)</td>
<td>0.043</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.9 (13)</td>
<td>97.2 (11)</td>
<td>0.047</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>146 (18)</td>
<td>142 (15)</td>
<td>0.006</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>88 (12)</td>
<td>84 (8)</td>
<td>0.001</td>
</tr>
<tr>
<td>SBP$_{ma}$ (mmHg)</td>
<td>138 (14)</td>
<td>132 (12)</td>
<td>0.0001</td>
</tr>
<tr>
<td>SBP$_{da}$ (mmHg)</td>
<td>87 (11)</td>
<td>83 (9)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Microalbuminuria (n, %)</td>
<td>69 (23)</td>
<td>21 (13)</td>
<td>0.01</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>73 (12)</td>
<td>76 (11)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Data are presented as average (standard deviation)

Table 4
(A) and (B) Multivariate linear linear regression analysis for LVM$_{BSA}$ and LVM$_{Bheight}$ as the dependent variable.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta-coefficient</th>
<th>CI 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) LVM$_{BSA}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.216</td>
<td>0.08–0.35</td>
<td>0.002</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>19.55</td>
<td>16.1–23.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>24-h systolic BP</td>
<td>0.640</td>
<td>0.51–0.77</td>
<td>0.0001</td>
</tr>
<tr>
<td>lg-UAE</td>
<td>4.60</td>
<td>1.42–7.78</td>
<td>0.005</td>
</tr>
<tr>
<td>(B) LVM$_{Bheight}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>0.148</td>
<td>0.08–0.22</td>
<td>0.0001</td>
</tr>
<tr>
<td>24-h systolic BP</td>
<td>0.331</td>
<td>0.26–0.40</td>
<td>0.0001</td>
</tr>
<tr>
<td>lg-UAE</td>
<td>2.1</td>
<td>0.49–3.74</td>
<td>0.011</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>0.302</td>
<td>0.23–0.38</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

SBP$_{da}$ ≥ 130 mmHg and presence of microalbuminuria were independent predictors of LVM$_{BSA}$. waist circumference did not enter the model.

Variables related to LVH adjusted by height$^{2,7}$

In contrast, when LVM$_{Bheight}$ was introduced as the dependent variable (Table 5B), age, male gender, SBP$_{da}$ ≥ 130 mmHg, microalbuminuria and abdominal obesity were all associated with LVM$_{Bheight}$. Furthermore, waist circumference not only retained its significant association with LVM$_{Bheight}$ (OR 3.56; CI 95%; 1.88–6.74; p < 0.0001), but also presented higher odds ratios than did SBP$_{da}$ (OR 2.32; CI 95%; 1.5–3.58; p < 0.0001).

Interaction of ambulatory systolic BP and obesity

Table 6 shows the prevalence of LVM$_{Bheight}$ according to SBP$_{da}$ and presence or absence of abdominal obesity. The prevalence of LVH$_{Bheight}$ is highest in patients with SBP$_{da}$ > 130 mmHg and abdominal obesity. Nevertheless, Fig. 1 shows that the effect of SBP$_{da}$ on LVH$_{Bheight}$ differs between patients with and without abdominal obesity. The effect of elevated SBP$_{da}$ on abdominal obesity, although increasing the prevalence of LVH$_{Bheight}$, is not simply additive, suggesting a different kind of interaction. In order to quantify this effect, we introduced the interaction SBP$_{da}$ × waist circumference in the multivariate logistic model, adjusting for age, gender and presence of microalbuminuria, resulting in a significant interaction. Of note, the OR of the interaction is 0.47 (Table 5B: OR 0.47; CI 95%; 0.22–0.99; p < 0.048). That observation means that the higher the values of BP or abdominal obesity, the lower is the effect of their interaction to further increase the prevalence of LVH, compared with the isolated effect of each factor on LVH.

Relative wall thickness

Table 6 shows the prevalence of LV geometric patterns. Only 22.1% of patients, when LVM was adjusted to BSA, and 14.1% when adjusted to height$^{2,7}$, presented a completely normal LV structure. The most prevalent geometric pattern in BSA-adjusted...
Table 5  
(A) and (B) Multivariate logistic regression analysis for LVH_{BSA} and for LVH_{height} as the dependent variable.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>LVH_{BSA} %</th>
<th>ORm*</th>
<th>CI 95%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(A) LVH_{BSA}</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>363</td>
<td>40.3</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>387</td>
<td>59.7</td>
<td>1.42</td>
<td>1.04–1.93</td>
<td>0.027</td>
</tr>
<tr>
<td>SBP_{24h} &lt; 130 mmHg</td>
<td>196</td>
<td>22.4</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>554</td>
<td>46.8</td>
<td>2.55</td>
<td>1.73–3.75</td>
<td>0.0001</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal UAE</td>
<td>631</td>
<td>37.1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased UAE</td>
<td>119</td>
<td>58.0</td>
<td>1.95</td>
<td>1.29–2.94</td>
<td>0.002</td>
</tr>
</tbody>
</table>

| (B) LVH_{height} |     |             |      |        |      |
| Age |     |             |      |        |      |
| Female | 363 | 55.6        | 1    |        |      |
| Male | 387 | 67.4        | 1.55 | 1.12–2.14 | 0.008 |
| SBP_{24h} < 130 mmHg | 198 | 46.9        | 1    |        |      |
|          | 554 | 67.0        | 2.32 | 1.50–3.58 | 0.0001 |
| Microalbuminuria |     |             |      |        |      |
| Normal UAE | 631 | 59.1        | 1    |        |      |
| Increased UAE | 119 | 75.6        | 1.85 | 1.15–2.98 | 0.011 |
| Waist circumference | | | | | |
| Waist ≤ 88 cm/102 | 461 | 55.1        | 1    |        |      |
| Waist > 88 cm/102 | 289 | 72.3        | 3.56 | 1.88–6.74 | 0.0001 |
| Interaction SBP_{24h}/waist circumference | | | | | 0.47 | 0.22–0.99 | 0.048 |

Adjusted by age; LVH_{BSA}, left ventricular hypertrophy adjusting for BSA; LVH, left ventricular hypertrophy; ORm, odds ratio multivariate; SBP, systolic blood pressure; UAE, urinary albumin excretion; increased UAE*, the cut-off values for the presence of microalbuminuria were ≥22 mg/g creatinine in men and ≥31 mg/g creatinine in women. LVH_{height}, left ventricular hypertrophy adjusting for height^{2,7}.

Table 6  
Ventricular geometry.

<table>
<thead>
<tr>
<th>LVM/BSA</th>
<th>All</th>
<th>Men</th>
<th>Women</th>
<th>p</th>
<th>OR/CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal, n (%)</td>
<td>166 (22.1)</td>
<td>57 (14.7)</td>
<td>109 (30.0)</td>
<td>0.0001</td>
<td>OR: 0.40/0.28–0.58</td>
</tr>
<tr>
<td>Concentric remodelling, n (%)</td>
<td>281 (37.5)</td>
<td>149 (38.5)</td>
<td>132 (36.4)</td>
<td>ns</td>
<td>/OR: 1.68/1.23–2.29</td>
</tr>
<tr>
<td>Eccentric hypertrophy, n (%)</td>
<td>244 (32.5)</td>
<td>147 (38.0)</td>
<td>97 (26.7)</td>
<td>0.001</td>
<td>0.048/0.28–0.58</td>
</tr>
<tr>
<td>LVM/height(^{2,7})</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal, n (%)</td>
<td>106 (14.1)</td>
<td>38 (9.3)</td>
<td>70 (19.3)</td>
<td>0.001</td>
<td>OR: 0.43/0.28–0.66</td>
</tr>
<tr>
<td>Concentric remodelling, n (%)</td>
<td>181 (24.1)</td>
<td>90 (23.3)</td>
<td>91 (25.1)</td>
<td>ns</td>
<td>1.64/1.23–2.19</td>
</tr>
<tr>
<td>Concentric hypertrophy, n (%)</td>
<td>351 (46.8)</td>
<td>204 (52.7)</td>
<td>147 (40.5)</td>
<td>0.001</td>
<td>0.43/0.28–0.66</td>
</tr>
<tr>
<td>Eccentric hypertrophy, n (%)</td>
<td>112 (14.9)</td>
<td>57 (14.7)</td>
<td>55 (15.2)</td>
<td>ns</td>
<td>1.64/1.23–2.19</td>
</tr>
</tbody>
</table>

LVM, left ventricular mass; BSA, body surface area; OR, odds ratio; CI, confidence intervals.

LVM was concentric remodelling (37.5%), followed by concentric hypertrophy (32.5%) and eccentric hypertrophy (7.9%). In height\(^{2,7}\)-adjusted LVM almost half of the patients (46.8%) presented concentric hypertrophy as the most prevalent geometric alteration.

A normal geometric structure was significantly less prevalent in men than in women (14.7% vs. 30.0%, p = 0.0001; OR: 0.40; CI 95%: 0.28–0.58), the prevalence of concentric hypertrophy, however, was significantly higher in men than in women (38.0% vs. 26.7%, p = 0.001; OR: 1.68; CI 95%: 1.23–2.29). The association between normal geometry and female gender as well as between concentric hypertrophy and male gender did not change when LV mass was adjusted to height\(^{2,7}\).

Discussion

The present study analyses the relationship between abdominal obesity, blood pressure and left ventricular hypertrophy in...
hypertension, showing a positive but not merely additive interaction between SBP_{24h} and obesity. SBP_{24h} is an important predictor of LVH, independent of adjusting for BSA or height, whereas the impact of obesity on the heart strongly depends on the criteria used to adjust LVM. After adjusting for height \(^2,7\), increased waist circumference as a marker of abdominal obesity represents the strongest predictor of LVH and interacts with BP. Obesity, however, is almost completely displaced by ambulatory systolic BP after adjusting LVM for BSA.

**Prevalence of LVH**

It is well known that LVH is the most prevalent subclinical target organ lesion in hypertension.\(^5,14\) Our study included only patients with recently diagnosed hypertension to investigate the impact of obesity and blood pressure on LVH at the very beginning of the natural history of hypertension and to avoid the confounding effect of concomitant antihypertensive treatment in long-standing hypertensive patients. Not surprisingly, baseline BP values were only mildly elevated. A main result of our study was that the prevalence of LVH_{right} exceeds that of LVH_{LSA} by almost 50% in newly diagnosed hypertensives. LVH prevalence varied from 40.4%, when adjusting for BSA (LVH_{LSA}) to 61.7%, when adjusting for height \(^2\) (LVH_{right}). Echocardiographic LVH prevalence in the literature differs to a great extent depending on the selection of study participants, the proportion of hypertensive patients, the severity and treatment of hypertension and the criteria used to define LVH, ranging from as low as 12\(^2,15\) in borderline hypertension indexing for BSA to 63% in mild to moderate hypertension according to Framingham (height)\(^16\) or even 77% in hypertensive patients with LV hypertrophy by ECC\(^11\) and normalization for height. Studies previously performed in our environment\(^12\) have shown comparable, although slightly higher prevalences of LVH, probably because the VITA-study included mostly treated hypertensives, as well as slightly lower prevalences in younger patients in the Hospitalist Study.\(^18\)

**Differences between patients with LVH depending on partition values**

In line with previous studies that included larger number of patients,\(^19\) almost all the patients categorized as hypertrophic by BSA simultaneously presented LVH by height\(^2,7\). In contrast, 162 patients classified as having LVH only by height\(^2,7\) had lower LVM, were more often female, obese, they had lower systolic and diastolic BP values and a lower prevalence of extracardiac renal lesion than did hypertrophic patients by both criteria. Nevertheless, compared to patients without LVH, this group ranks in an intermediate position, with more risk factors than non-hypertrophic patients, but less than patients classified as hypertrophic by either criterion. This finding has important consequences for daily clinical practice. The Guidelines for the Management of Arterial Hypertension of theESH underscore the relevance of subclinical target organ damage for estimating the global cardiovascular risk of patients beyond BP values. Suárez et al.\(^20\) reclassified up to 30% of 197 patients of low to intermediate risk into the high-risk category after detecting LVH in echocardiography. Correcting LVM for height\(^2,7\) would allow for detecting subclinical LVH in an even greater and significant proportion of patients who otherwise would be classified as low risk, at least in the early stages of the evolution of hypertension.

**Role of obesity in LVH**

Variations of LVM secondary to body size and gender are reduced correcting LVM for BSA,\(^21\) but the impact of overweight is underestimated.\(^7,22\) Levy et al.\(^23\) proposed adjusting for height from population-based data to isolate and evaluate the separate role of obesity. Despite that, residual variability among normal subjects seems to be best accounted for by indexing for allometric height-based adjustments.\(^24\) In recent years, indexing to height\(^2,7\) has been increasingly used to stratify risk in patients,\(^5,25\) especially in obese subjects. We therefore performed our study comparing both approaches, indexing to BSA and to height\(^2,7\).

Obesity has been shown to be a potent stimulus for LVH,\(^22,26\) even, more important than BP itself.\(^16,27\) There is little doubt that obesity contributes to LVH independent of BP,\(^28\) but it is still a matter of controversy to what extent and in which way obesity interacts with BP to increase LVM. According to Messerli et al.,\(^29\) obesity and BP increase LVM by different mechanisms that may merge in the same patient. Hammond found a strong and independent but only additive effect of obesity on BP comparing 624 normotensive, borderline and hypertensive patients.\(^30\) Similar results confirming addition but not interaction between obesity and BP were confirmed in the TOMHS-study\(^11\) and by Lauer et al.\(^32\) That notwithstanding, Grotti et al.\(^33\) postulated a synergistic and interactive effect of obesity and BP in such a way that obesity amplifies the effect of BP to produce LVH. Obesity was defined by BMI and the positive interaction between obesity (normal: BMI < 27 kg/m\(^2\), overweight: BMI 27–30 kg/m\(^2\), obesity: BMI > 30 kg/m\(^2\)) and BP was inferred from the fact that obesity and overweight increased the slope of the relationship between systolic BP and LVM indexed to height in the first power, which illustrated in a two-dimensional figure with LVM and BP as continuous variables. This synergistic effect was not quantified and no specific statistical method to calculate interaction was given. In contrast, in our study, multivariate logistic analysis demonstrates an interaction between obesity, measured as pathological abdominal, sex-adjusted waist circumference, and BP with an estimated OR of 0.47. This suggests that the interaction, although positive, is about 50% lower than expected, if the OR of the interaction had been equal or greater than 1.

There might be several explanations for this discrepancy. Gottdiener’s patients are part of a larger cohort\(^7\) that included only men, they were older (59 versus 47 years) and, to a great extent, previously treated (66%). They had higher systolic and diastolic BP (SBP 152 mmHg, DBP 99 mmHg versus SBP 141 mmHg and DBP 85 mmHg in our study). Furthermore, ambulatory BP was not measured, and the definition of compared variables was slightly different: LVM was corrected for height in the first power, and normal weight was considered below 27 kg/m\(^2\). Instead, we adjusted for height\(^2,7\), obesity was defined as increased abdominal circumference according to generally accepted cut-off values, and we related LVM with ambulatory systolic BP, both as dichotomous variables in a multivariate logistic regression analysis.

The interaction of obesity and blood pressure may have important clinical implications for the treatment of individual patients. The odds ratio of the interaction variable is below one, suggesting that the LVH-promoting effect of high blood pressure might be attenuated in obese patients in whom abdominal obesity may play an increasing role in causing LVH. The message for daily clinical practice could be that the reversal of obesity might be more important than the addition of antihypertensive drugs in never treated obese patients with uncontrolled hypertension. And conversely, in lean hypertensive patients, hypertension may be comparatively more effective at producing LVH than in obese patients. Accordingly, they are a more suitable target to address with antihypertensive drugs.

**Advantages of indexing LVM for body surface area**

The role of obesity in LVH when indexing LVM for BSA seems to be negligible because weight itself is included in the mathematical
formula for calculating BSA. This fact is often referred to as underestimation of obesity and, therefore, height is being increasingly recommended as a correction value. Nevertheless, it can be argued that indexing LVM for BSA makes it possible to isolate the effect of BP on not only the pathogenesis of LVH, but also more importantly, in studies of the regression of LVH. Medical progress has developed an arsenal of antihypertensive drugs, but we do not possess any efficacious treatment for obesity, which tends to be constant and stable over long periods of time in both individuals, as well as in groups of patients. When studying LVH and its regression or progression, obesity might represent an unpleasant confounding and constant, unavoidable factor. In fact, whereas most population-based studies on the prevalence of LVH have been done adjusting for both BSA and height, the vast majority of longitudinal studies of regression of LVH are carried out adjusting for BSA. Recently, Cuspidi et al. reviewed published randomized trials evaluating the effect of antihypertensive treatment on LVH. Out of 39 eligible studies only one study used height as a correction criterion for LVM. The remaining 33 studies adjusted LVM for BSA, although using as many as 19 criteria. Five studies did not provide any definition of LVM.

Type of LVH

Our study confirms the results of previous studies, underlining the high prevalence of alterations of cardiac structure in hypertension. Between 77% in BSA adjusted LVM and 86% in height adjusted LVM of our patients presented some alteration of ventricular geometry. Eccentric hypertrophy has been described as the most frequent pattern of geometric alteration in hypertension.33 In our group of exclusively untreated hypertensives, however, concentric hypertrophy was more prevalent than eccentric hypertrophy. Besides, concentric remodelling exceeded the prevalence of concentric hypertrophy in our patients, suggesting a time-linked dynamic transition from concentric remodelling over concentric hypertrophy to eccentric hypertrophy, so that in earlier stages of hypertension concentric hypertrophy may precede the development of eccentric hypertrophy. A further argument supporting this hypothesis results from data in advanced hypertension, as represented by patients included in the LIFE study,34 where concentric remodelling was much less frequent (10.5%) than true hypertrophic alterations, such as concentric (23.9%) or eccentric hypertrophy (46.5%). Additional studies are needed to test this hypothesis.

Information on gender-related LVH patterns is scarce. A recent review of the literature that included 4384 patients from the general population as well as treated and untreated hypertensives did not find significant gender differences in LV geometry.35 Our results show a significantly higher prevalence of concentric LVH in men than in women, in line with the significant gender differences described also for LV mass in our study, probably due to the fact that we analyzed patients in early stages of hypertension. Interestingly, this finding was identical when LVM was adjusted to BSA and to height.2,7

Limitations of our study

The results of our study should be interpreted with caution because our results are hospital-based and not population-based. Although our study obviates the confounding effect of previous pharmacological treatment, our patients probably carry an elevated cardiovascular risk compared to the normal population because of associated hypertensive disease. Besides, the relationship between LVM and cardiovascular risk is linear,32 and the cut-off values to define LVH in our study are necessarily arbitrary. Furthermore, very recently, Chirinos et al.36 suggested a new indexing coefficient, height1.7, comparing echocardiographic and MRI-based measurements. We limited the analysis to the most used and established partition values for BSA and height2,7, but cannot exclude different results with different criteria. Our echocardiograms were not reviewed by a central institution as we describe the daily clinical practice, but they were always performed by the same echocardiographers at the same centre, and under the same conditions.

Conclusions

Abdominal obesity is the strongest predictor of LVH in never treated hypertensives only when LVM is indexed to height2,7, leading to a higher prevalence of LVH than adjusting for BSA does. Obesity interacts with systolic BP24h in an additive but not strictly synergistic manner. Systolic BP24h is the most important determinant of LVH when indexing for BSA. Concentric remodelling seems to be the most prevalent alteration of ventricular geometry in early stages of hypertension.

Conflict of interest

The authors declare no conflict of interest.

References


