Electrocardiographic Criteria for Left Ventricular Hypertrophy and Cardiovascular Risk in Hypertensives. VIIDA Study

José R. González-Juanatey,[a] Luis Cea-Calvo,[b] Vicente Bertomeu,[c] and Joaquín Aznar,[d] on behalf of VIIDA study researchers

[a]Servicio de Cardiología, Hospital Clínico Universitario, Facultad de Medicina, Santiago de Compostela, La Coruña, Spain
[b]Departamento de Investigación Clínica, Merck Sharp & Dohme of Spain
[c]Servicio de Cardiología, Hospital Universitario San Juan, Alicante, Spain
[d]Servicio de Cardiología, Hospital Real y Provincial Nuestra Señora de Gracia, Zaragoza, Spain

Introduction and objectives. To determine whether Cornell and Sokolow-Lyon criteria identify different groups of patients with left ventricular hypertrophy (LVH), and whether there is a relationship between hypertrophy severity and the prevalence of cardiovascular disease.

Methods. Cross-sectional multicenter study carried out in cardiology departments on hypertensive patients with electrocardiographic LVH, as defined by Cornell or Sokolow-Lyon criteria. Blood pressure (BP) and clinical and laboratory data were recorded. The study population was divided into quartiles according to electrocardiographic findings to enable relationships with cardiovascular disease to be evaluated.

Results. Overall, 3074 patients with LVH were studied: 978 (31.8%) met both LVH criteria, 1244 (40.5%) met Cornell criteria only, and 852 (27.7%) met Sokolow-Lyon criteria only. Fulfillment of Sokolow-Lyon criteria was associated with male gender, a low body mass index (BMI), a low prevalence of diabetes, and a high prevalence of myocardial infarction. Fulfillment of Cornell criteria was associated with female gender, a high BMI, and a high prevalence of diabetes. Fulfillment of both criteria was associated with poor BP control and a high prevalence of heart failure. Associations were observed between LVH severity and the prevalence of cardiovascular disease: the adjusted odds ratio for the upper versus the lower quartile was 1.65 (*P*=.011) for Sokolow-Lyon criteria, 1.59 (*P*=.014) for Cornell criteria, and 2.03 (*P*=.001) for both combined.

Conclusions. Sokolow-Lyon and Cornell criteria identify patients with different high-risk cardiovascular risk profiles. Consequently, it would be preferable to use both criteria as this would increase the detection rate of electrocardiographic LVH. Moreover, there is a relationship between the severity of electrocardiographic LVH and the prevalence of established cardiovascular disease.

Key words: *Arterial hypertension. Electrocardiography. Hypertrophy. Cardiovascular disease.*

Criterios electrocardiográficos de hipertrofia ventricular izquierda y perfil de riesgo cardiovascular en hipertensos. Estudio VIIDA

Introducción y objetivos. Evaluar si los criterios de Cornell y Sokolow-Lyon permiten identificar a los pacientes con hipertrofia ventricular izquierda (HVI) de distinto perfil y si hay asociación entre la severidad de la hipertrofia y la prevalencia de enfermedad cardiovascular.

Métodos. Estudio transversal y multicéntrico, en consultas de cardiología, en pacientes hipertensos con HVI por Cornell o Sokolow-Lyon. Se recogieron los valores de la presión arterial (PA), así como los datos clínicos y analíticos. Se dividió a la población en cuartiles según los complejos electrocardiográficos para valorar la asociación con la enfermedad cardiovascular.

Resultados. En total fueron analizables 3.074 pacientes con HVI; 978 pacientes (31,8%) cumplieron ambos criterios, 1.244 (40,5%) cumplieron sólo los criterios de Cornell y 852 (27,7%), sólo los de Sokolow-Lyon. La positividad por Sokolow-Lyon se asoció con el sexo masculino y un menor índice de masa corporal (IMC), así como con una menor prevalencia de diabetes y mayor de infarto de miocardio. La positividad por Cornell se asoció con el sexo femenino, un mayor IMC y una mayor prevalencia de diabetes. La positividad por ambos se asoció con un peor control de la PA y una mayor prevalencia de insuficiencia cardiaca. Se observó asociación entre la mayor severidad de la HVI y la prevalencia de enfermedad cardiovascular (*odds ratio* ajustada [ORa] para el cuartil superior respecto al inferior = 1,65; p = 0,011, para Sokolow-Lyon; ORa =

The VIIDA study received unconditioned financial support from Merck Sharp & Dohme of Spain.

Correspondence: Dr. J.R. González-Juanatey.
Servicio de Cardiología. Hospital Clínico Universitario.
A Choupana, s/n. 15706 Santiago de Compostela. A Coruña. España.
E-mail: jose.ramon.gonzalez.juanatey@sergas.es

Received March 17, 2006.
Accepted for publication November 27, 2006.

ABBREVIATIONS

ECG: electrocardiogram
AHT: arterial hypertension
LVH: left ventricular hypertrophy
BMI: body mass index
BP: blood pressure

1,59; p = 0,014, para Cornell, y ORa = 2,03; p = 0,001, para la suma).

Conclusiones. Los criterios de HVI de Sokolow-Lyon y Cornell identifican a pacientes de distinto perfil y elevado riesgo cardiovascular, por lo que es recomendable utilizar ambos para aumentar la detección de la HVI electrocardiográfica. Además, hay relación entre severidad de la HVI electrocardiográfica y la prevalencia de enfermedad cardiovascular establecida.

Palabras clave: *Hipertensión arterial. Electrocardiografía. Hipertrofia. Enfermedad cardiovascular.*

INTRODUCTION

Left ventricular hypertrophy (LVH) presents high prevalence in patients with arterial hypertension (AHT). Diagnosis, by electrocardiogram (ECG)[1] and echocardiogram,[2,3] identifies significantly increased risk of cardiovascular complication both in patients with AHT and in those with associated diseases (ischemic heart disease, kidney failure, etc).[4-6] Presence of LVH increases the risk of heart failure, ischemic heart disease, sudden death, atrial fibrillation, and stroke. In particular, hypertensive LVH and stroke are closely related and association is independent of blood pressure.[7] Patients with LVH have a greater risk of developing atrial fibrillation and this mechanism may explain their being at greater risk of stroke.[8]

Clinically, diagnosis of LVH is fundamental in risk stratification in hypertensives and LVH regression should be a therapeutic objective.[9] Guidelines to clinical practice in AHT include identifying LVH as a consideration in patient risk stratification.[9-11]

Echocardiography is the standard diagnostic technique for LVH but lack of availability limits its use. The ECG is less sensitive in LVH diagnosis but is an extremely useful tool in outpatient clinics. Although many ECG criteria for LVH have been described,[12-16] Sokolow-Lyon criteria[12] and those proposed by Cornell University[13] (Cornell criteria) are the most widely used in clinical practice. Both show high specificity in LVH diagnosis but their sensitivity is limited. Although the prevalence of LVH in the hypertense population has been analyzed using these criteria, in Spain the question of whether both criteria identify groups of patients with LVH with distinctive clinical characteristics, has not been described.

Our objective was to analyze, in a broad-based sample of patients with LVH (VIIDA study), whether Sokolow-Lyon criteria, Cornell criteria, or both, identify groups of patients with different clinical characteristics, and learn whether an association exists between LVH severity (voltage magnitude criteria) and presence of complications of cardiovascular disease. The primary objective of conducting the VIIDA study was to learn about LVH prevalence and the clinical characteristics of patients with LVH in the context of outpatient cardiology clinics in Spain.

METHODS

The VIIDA study is a cross-sectional, multicenter, epidemiologic study, conducted in outpatient cardiology clinics across Spain. It was designed by the Hypertension and Outpatient Cardiology sections of the Spanish Society of Cardiology and approved by an independent Clinical Research Ethics Committee; 200 cardiologists participated in the study. Patients were enrolled from April 2003 thru November 2004 (on 3 different days during the period, at 6-month intervals). Following written consent, we included patients with AHT, with no age-limit, whether or not they had a history of cardiovascular disease. We collected data on clinical history variables and, when necessary, patients underwent complementary examinations.

We screened consecutive hypertense patients attending clinic. An initial questionnaire elicited data on history of AHT, age, gender, weight, build, cardiovascular risk factors, and presence of cardiovascular disease. Presence of LVH was defined by Sokolow-Lyon ECG criteria (R wave in V_5 through V_6+S wave in V_1 >35 mm), Cornell voltage criteria (R wave in aVL+S wave in V_3 >20 mm in women or >28 mm in men), or both. Patients presenting electrocardiographic LVH underwent a complete study to obtain demographic and anthropometric data, cardiovascular risk factors and presence or history of cardiovascular disease (myocardial infarction, angina pectoris, intermittent claudication, heart failure, and stroke). Biochemical data were obtained from samples taken in the 6 months prior to data collection and, if unavailable, analyses were performed at the time.

Blood pressure (BP) was measured according to standardized norms, with a mercury sphygmomanometer. Patients were seated and, after 5 minutes rest, BP was measured 3 times, at 2-minute intervals. We calculated the mean of the last 2 measurements and this was considered the patient's BP.

Statistical Analysis

Sample size was calculated to achieve our primary objective: to estimate prevalence of electrocardiographic

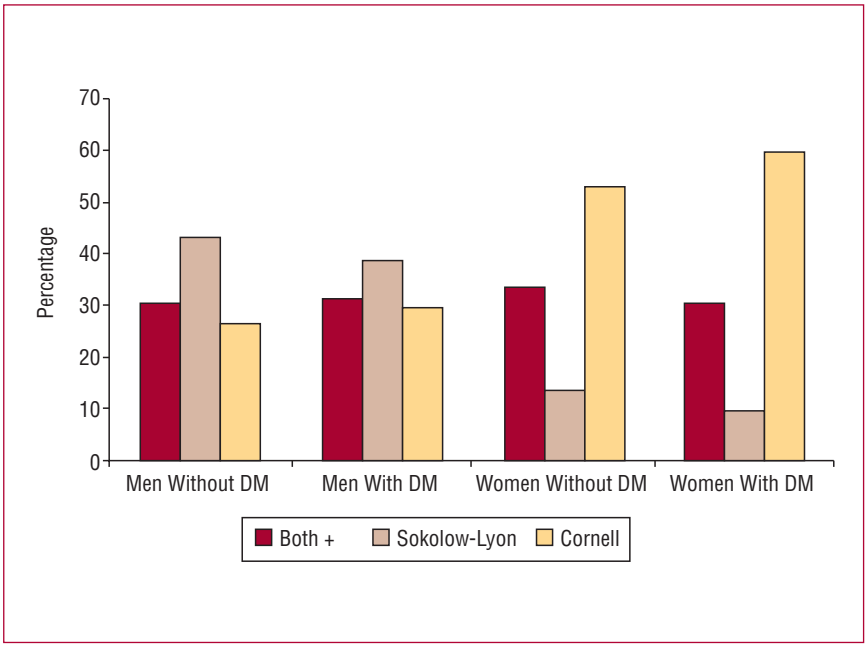

Figure 1. Percentage of patients positive for each LVH criterion, by gender and diabetes mellitus. VIIDA study.
DM indicates diabetes mellitus; LVH, left ventricular hypertrophy.

LVH in the hypertense population. We enrolled 3074 patients and adopted 95% confidence intervals and 1.5% sample error, for final prevalence of LVH of 25%.

Qualitative variables are given with frequency distribution. Quantitative variables are summarized as mean (SD). We determined relationships between qualitative variables with χ^2 or Fisher exact test. We analyzed the behavior of each quantitative variable for each of the independent variables using analysis of variance (ANOVA). Statistical significance was later adjusted with the Bonferroni correction in both cases.

To evaluate the relationship between LVH severity and presence of established cardiovascular disease, the value of each LVH criterion was divided in intervals according to its distribution quartiles. We constructed logistic regression models to explain relationships between cardiovascular disease and LVH severity for each criterion. We present the adjusted odds ratio (aOR) and 95% confidence intervals (CI). Variables were selected according to criteria of biological relevance.

In all cases, we tested variable distribution against the theoretical models and contrasted the hypothesis of homogeneity of variance. In all contrasts of hypothesis, the null hypothesis was rejected with a type I error or alpha error <.05. Statistical analysis was with SPSS 12.

RESULTS

Percentage of Patients Meeting the Different Criteria

Of 16 123 screened patients, 4037 (24.6%) had electrocardiographic LVH and for 3074 (76.1%) we had specific measurements of the complexes needed to evaluate Cornell or Sokolow-Lyon criteria. Of these, 978 patients (31.8%) fulfilled both criteria, 1244 (40.5%) met Cornell criteria only and 852 (27.7%), Sokolow-Lyon criteria only.

Some 30.6% of men and 33.2% of women fulfilled both criteria; 42.2% of men and 11.9% of women met Sokolow-Lyon criteria and 27.3% of men and 54.9% of women met Cornell criteria. Percentages of patients stratified by gender and diabetes mellitus for each set of criteria appear in Figure 1. Cornell criteria were met by higher percentages of women and of patients with diabetes mellitus; in contrast, Sokolow-Lyon criteria were met by higher percentages of men and of patients without diabetes. Cornell criteria were met by a higher percentage of patients with greater body mass index (BMI); in contrast, Sokolow-Lyon criteria were met by a higher percentage of patients with lower (BMI), both in men and women (Figure 2).

Patient Characteristics

Table 1 presents characteristics of patients who met both criteria, Cornell criteria only, or Sokolow-Lyon criteria only. Table 2 presents prevalence of established cardiovascular disease and of each clinical entity in these patients.

Men accounted for 79.5% of patients who met Sokolow-Lyon criteria only, whereas women accounted for 64.8% of patients who met Cornell criteria only. When compared with the rest of the sample, characteristics of patients meeting Cornell criteria only, included a slightly higher mean age, higher mean BMI, a greater percentage of women and greater prevalence of diabetes mellitus and obesity (BMI >30). When

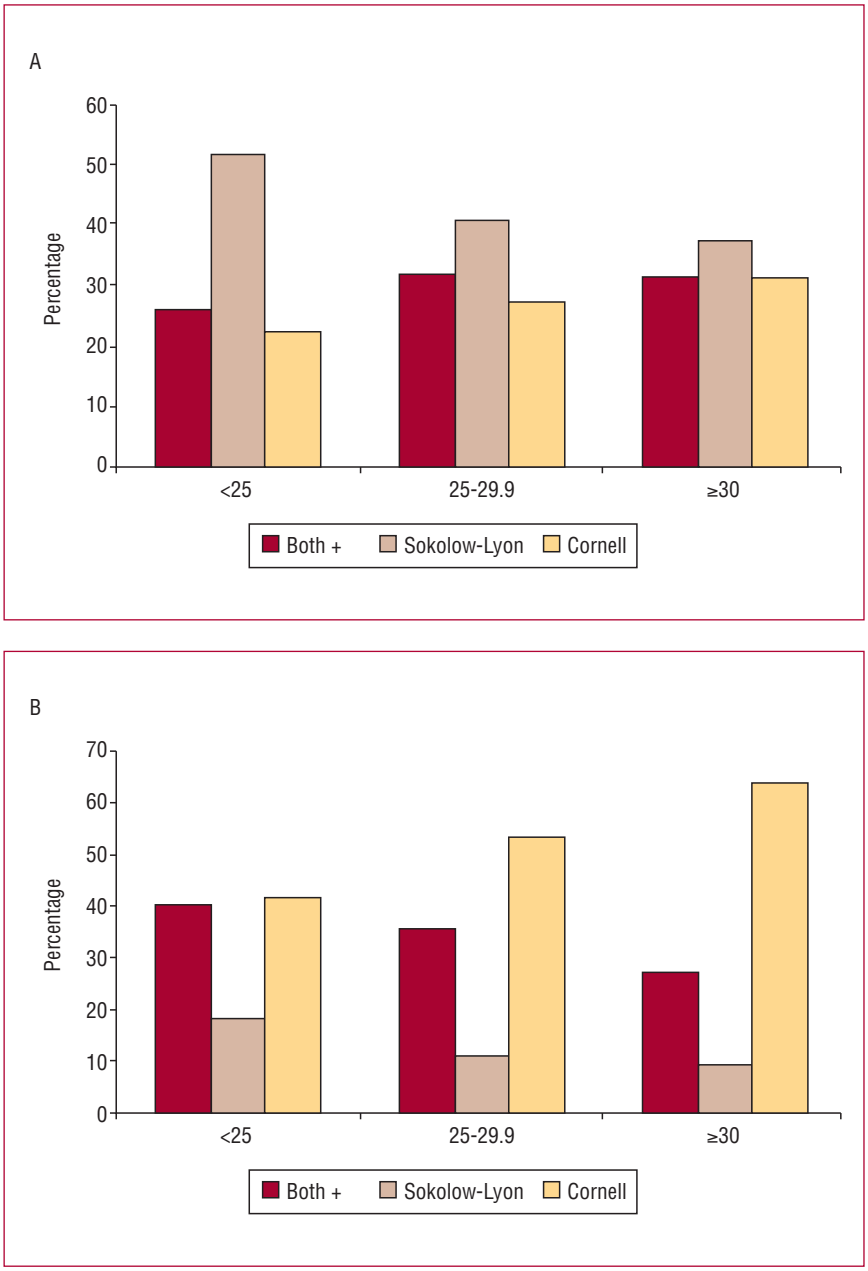

Figure 2. Percentage of patients positive for each LVH criterion, stratified by BMI. VIIDA study. A indicates men; B, women; LVH, left ventricular hypertrophy; BMI, body mass index.

compared with patients meeting Sokolow-Lyon criteria only, prevalence of heart failure was greater in this group. Characteristics of patients who met Sokolow-Lyon criteria only were male gender, lower BMI, lower percentage of diabetes, and greater prevalence of antecedents of myocardial infarction (Table 1).

Patients meeting both criteria presented higher BP, greater prevalence of heart failure; this group also included a lower percentage of controlled patients. We observed no differences in overall prevalence of established cardiovascular disease between the 3 groups. In a multivariate model including age, gender, systolic blood pressure (SBP), diastolic blood pressure (DBP), diabetes mellitus, BMI, and myocardial infarction, presence of LVH as defined by Cornell criteria (aOR=1.43; 95% CI, 1.08-1.89; *P*=.013) and both criteria (aOR=2.11; 95% CI, 1.59-2.81; *P*<.001) associated significantly with presence of heart failure, by comparison with presence of LVH as defined by Sokolow-Lyon criteria.

Relationship Between Hypertrophy Severity and Established Cardiovascular Disease

To estimate the impact of LVH severity on prevalence of established cardiovascular disease we defined quartiles according to Sokolow-Lyon voltages, Cornell voltages,

TABLE 1. Characteristics of Hypertense Patients With Left Ventricular Hypertrophy According to the Criteria fulfilled. VIIDA Study*

	Sokolow-Lyon Positive (n=852)	Cornell Positive (n=1244)	Both Positive (n=978)	P†
Age, y	66.9 (11.4)	69.7 (10.5)	67.5 (10.8)	B
Gender				
Women	20.5	64.8	49.8	A
Men	79.5	35.2	50.2	A
BMI	27.0 (3.6)	28.6 (4.2)	27.6 (3.9)	A
<25	29.3	17.0	22.7	A
25-29.9	45.0	43.0	47.3	A
≥30	25.7	40.0	30.0	A
Smokers	17.0	8.2	17.3	B
Diabetes mellitus	21.0	30.6	26.0	C
SBP, mm Hg	150.3 (20.3)	148.2 (21.2)	153.5 (19.1)	D
DBP, mm Hg	84.3 (11.9)	82.8 (12.8)	87.5 (12.2)	D
Controlled BP‡	21.9	22.8	14.4	D
GFR <60 mL/min/ 1.73 m^2	27.2	42.7	38.4	A

*BMI indicates body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate. Values are given as mean (SD) or percentage
†*P*<.05 was considered statistically significant with the following provisos: A, statistically significant differences exist between the 3 categories; B, significant differences exist between Cornell positive patients and the other 2 groups; C, significant differences exist between Sokolow-Lyon positive patients and the other 2 groups; D, significant differences exist between both criteria positive patients and the other 2 groups.
‡Blood pressure <140/90 mm Hg, and in patients with diabetes <130/80 mm Hg.

TABLE 2. Prevalence of Established Cardiovascular Disease in Hypertense Patients With Left Ventricular Hypertrophy According to the Criteria Fulfilled. VIIDA Study*

	Sokolow-Lyon Positive (n=852)	Cornell Positive (n=1244)	Both Positive (n=978)	P†
Established cardiovascular disease	59.8	59.1	59.6	A
Myocardial infarction	30.2	21.9	27.4	B
Angina pectoris	37.9	37.5	37.0	A
Stroke	13.8	10.6	15.4	B
Peripheral vascular disease	13.6	7.9	15.7	B
Heart failure	25.9	33.3	41.1	C
Atrial fibrillation	23.7	22.7	27.1	A

*Values are given as percentages.
†*P*<.05 was considered statistically significant with the following provisos: A, no differences exist between the 3 groups; B, significant differences exist between Cornell positive patients and the other 2 groups; C, significant differences exist within the 3 groups.

and the sum of both. Patient characteristics and manifestations of cardiovascular disease in each quartile appear in Tables 3 A-C.

Characteristics of patients who met Sokolow-Lyon criteria appear in Table 3A. Comparison of higher versus lowest quartile patients shows the former were slightly younger, more often men, had higher BP levels and less BP control, lower BMI and lower percentages of obesity, diabetes, and abnormal kidney function. Upper quartile patients also presented greater prevalence of myocardial infarction, stroke, peripheral vascular disease, and atrial fibrillation. A multivariate model adjusted for age, gender, BP, BMI, and diabetes showed patients in the highest quartile had a 65% greater prevalence of cardiovascular disease than patients in the lowest quartile (aOR=1.65; 95% CI, 1.12-2.43; *P*=.011).

Characteristics of patients who met Cornell voltage criteria appear in Table 3B. Comparison of higher versus lowest quartile patients show the former were less often controlled patients, had higher SBP and DBP, greater prevalence of diabetes, abnormal kidney function and established cardiovascular disease. Moreover, patients in the higher quartiles presented greater prevalence of myocardial infarction, peripheral vascular disease and heart failure. A multivariate model adjusted for age, gender, BP, BMI, and diabetes showed prevalence of cardiovascular disease was 59% greater in highest quartile patients versus lowest quartile patients (aOR=1.59; 95% CI, 1.09-2.30; *P*=.014); and 47% greater in third quartile versus lowest quartile patients (aOR=1.47; 95% CI, 1.00-2.17; *P*=.050).

Finally, we analyzed the severity of the 2 criteria combined (Table 3C). We divided the population in 4 quartiles according to the sum of the voltage criteria (sum R-aVL+S-V_3+S-V_1+R-V_{5-6}). Patients in the highest quartile were younger, more often men, had higher BP, a lower percentage of controlled BP and lower prevalence of obesity. Patients in the highest quartile had greater prevalence of established cardiovascular disease and antecedents of myocardial infarction, stroke, peripheral vascular disease, heart failure, and atrial fibrillation. In the multivariate model, adjusted for age, gender, BP, BMI, and diabetes, prevalence of established cardiovascular disease increased numerically with each quartile but only reached statistical significance when comparing patients in the highest versus lowest quartile (aOR=1.22; 95% CI, 0.78-1.92; *P*=.374 second vs lowest quartile; aOR=1.40; 95% CI, 0.91-2.17; *P*=.122 third vs lowest quartile, and aOR=2.03; 95% CI, 1.32-3.13; *P*=.001 highest vs lowest quartile).

DISCUSSION

The results of our study indicate that Cornell and Sokolow-Lyon diagnostic criteria enable us to identify hypertense patients with LVH with different epidemiologic and cardiovascular risk profiles. This

TABLE 3A. **Demographic Characteristics and Prevalence of Cardiovascular Diseases Stratified by Quartiles, in Patients With Left Ventricular Hypertrophy Defined by Sokolow-Lyon Criteria***

	Quartiles of Voltage of Sokolow-Lyon, mm				*P*
	≤25	26-36	37-40	>40	
Age, y	69.9 (10.4)	68.3 (10.7)	66.8 (10.9)	67.1 (11.7)	<.001
Men	30.8	53.7	66.0	61.3	<.001
SBP, mm Hg	149.2 (22.2)	150.9 (21.4)	151.7 (18.9)	152.8 (19.8)	.01
DBP, mm H	82.5 (13.1)	85.1 (12.5)	85.9 (11.6)	86.4 (12.4)	<.001
Controlled BP†	22.9	19.2	18.1	17.4	.015
BMI	28.9 (4.3)	27.7 (3.8)	27.4 (3.7)	27.1 (3.7)	<.001
Obesity	43.9	31.3	27.6	27.1	<.001
Diabetes mellitus	30.8	25.9	23.0	22.6	<.001
GFR <60 mL/min/1.73 m^2	42.5	37.2	29.6	36.6	<.001
Established cardiovascular disease	56.8	58.6	58.5	59.1	.776
Myocardial infarction	22.3	23.4	26.9	29.6	.010
Angina pectoris	36.5	41.1	36.8	35.4	.179
Stroke	10.7	14.6	13.4	15.9	.042
Peripheral vascular disease	7.9	14.2	13.2	16.1	<.001
Heart failure	30.5	34.0	30.4	34.8	.207
Atrial fibrillation	21.5	24.2	24.9	26.7	.072

*Values are given as mean (SD) or percentage. LVH indicates left ventricular hypertrophy; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate.
†<140/90 mm Hg, and in patients with diabetes <130/80 mm Hg

TABLE 3B. **Demographic Characteristics and Prevalence of Cardiovascular Diseases Stratified by Quartiles, in Patients With Left Ventricular Hypertrophy Defined by Cornell Criteria***

	Quartiles of Voltage of Sokolow-Lyon, mm				*P*
	≤21	26-26	27-31	>31	
Age, y	68.2 (10.9)	69.2 (10.1)	67.4 (11.2)	68.3 (10.9)	.009
Women	46.7	66.8	38.9	41.3	<.001
SBP, mm Hg	150.6 (21.7)	151.9 (20.0)	148.5 (19.7)	152.2 (20.5)	.01
DBP, mm Hg	83.9 (12.3)	85.4 (12.2)	84.5 (12.1)	85.3 (13.0)	.031
Controlled BP†	22.4	16.7	22.1	16.4	<.001
BMI	27.7 (4.2)	28.0 (4.1)	28.1 (3.8)	27.6 (3.7)	.036
Obesity	31.9	35.0	36.6	29.7	.004
Diabetes mellitus	23.0	27.6	28.5	26.8	.053
GFR <60 mL/min/1.73 m^2	31.9	43.1	33.3	38.7	<.001
Established cardiovascular disease	54.8	56.2	61.6	60.9	.010
Myocardial infarction	24.2	21.6	26.9	29.7	.007
Angina pectoris	34.7	35.3	40.8	38.1	.116
Stroke	12.6	11.3	14.3	13.6	.462
Peripheral vascular disease	10.1	8.2	14.3	15.9	<.001
Heart failure	24.3	31.0	34.3	41.0	<.001
Atrial fibrillation	23.4	26.1	23.0	24.2	.455

*Values are given as mean (SD) or percentage. LVH indicates left ventricular hypertrophy; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate.
†<140/90 mm Hg, and in patients with diabetes <130/80 mm Hg.

suggests the criteria are complementary and, therefore, we would recommend their combined use to detect LVH in a greater number of patients. In men, LVH diagnosis was preferably made using Sokolow-Lyon criteria whereas women more frequently fulfill Cornell criteria. However, with both criteria in isolation and thru combining them we observed an association between voltage magnitude and certain clinical characteristics, as well as with presence of established cardiovascular disease.

TABLE 3C. **Demographic Characteristics and Prevalence of Cardiovascular Diseases Stratified by Quartiles, in Patients With Left Ventricular Hypertrophy Defined by Combined Sokolow-Lyon and Cornell Criteria***

	Quartiles of Sokolow-Lyon and Cornell Voltage (Sum of Values for Both Criteria, mm)				*P*
	≤51	52-59	60-67	>67	
Age, y	69.8 (10.1)	67.9 (10.9)	68.2 (11.1)	67.0 (11.0)	<.001
Men	29.3	52.9	64.2	60.3	<.001
SBP, mm Hg	150.7 (22.2)	148.7 (21.6)	149.5 (18.9)	154.0 (19.5)	<.001
DBP, mm Hg	83.2 (13.2)	83.3 (12.4)	85.1 (11.7)	87.2 (12.6)	<.001
Controlled BP†	20.9	24.0	20.4	13.3	<.001
BMI	28.7 (4.2)	27.9 (4.0)	27.5 (4.0)	27.9 (3.5)	<.001
Obesity	41.2	32.2	30.3	28.9	<.001
Diabetes mellitus	28.3	25.8	25.6	25.1	.492
GFR <60 mL/min/1.73 m^2	42.3	33.1	33.0	40.0	<.001
Established cardiovascular disease	52.0	58.9	62.3	61.1	<.001
Myocardial infarction	21.4	22.8	28.6	29.5	.002
Angina pectoris	34.9	37.6	39.6	36.9	.398
Stroke	8.2	13.8	14.6	14.7	.002
Peripheral vascular disease	7.0	10.5	14.4	17.5	<.001
Heart failure	24.0	27.4	37.6	42.0	<.001
Atrial fibrillation	19.9	25.0	25.5	26.2	.015

*Values are given as mean (SD). LVH indicates left ventricular hypertrophy; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; GFR, glomerular filtration rate.
†<140/90 mm Hg, and in patients with diabetes <130/80 mm Hg

We believe these results are of special relevance as they identify clinical variables associated with presence of LVH as defined by different ECG criteria and establish a direct association between LVH severity, determined by voltage magnitude criteria, and prevalence of clinical cardiovascular disease. To our knowledge, it is the first time this association has been found thru the 2 voltage criteria most widely used in clinical practice. This indicates that voltage magnitude criteria, as well as being of value in LVH diagnosis, could be applied in hypertensives to improve determination of their cardiovascular and renal risk.

Various studies have analyzed prevalence of ECG-defined LVH in hypertense patients and report a 4%-18% range, as a function of the criteria used.[1] These studies coincide in that presence of LVH, by whichever criteria, is accompanied by a higher risk of cardiovascular complications. However, in Spain, no study has determined whether differences exist in demographic characteristics and in the relationship between different manifestations of cardiovascular disease according to which ECG criteria for LVH are fulfilled. We observed that LVH diagnosis was more prevalent in men when using Sokolow-Lyon criteria and in women, when using Cornell criteria. Moreover, we observed an association of both criteria with BMI and this was stronger in patients who met Cornell criteria and weaker in those who met Sokolow-Lyon criteria.

The LIFE study, conducted in patients with AHT and ECG-defined LVH, also found associations between LVH defined by Cornell criteria and women, presence of diabetes, and higher BMI. In patients with LVH defined by Sokolow-Lyon criteria, the opposite occurred.[17] Differences between women and men in thoracic geometry and heart position, and BMI, could be the principal determining factors. Moreover, given the known association between obesity and LVH,[18,19] Sokolow-Lyon criteria could identify with greater sensitivity patients in whom obesity does not play a substantial role in developing LVH. Similarly, excessive subcutaneous tissue in obese patients is likely to diminish voltage in the left precordial leads and reduce criterion sensitivity.

Several publications have analyzed the relationship between changes in voltage criteria for LVH and risk of cardiovascular complications in hypertensives and patients with high cardiovascular risk.[20-22] The Framingham study reported QRS complex voltage evolution in hypertense patients was associated with cardiovascular risk, and that patients with reduced voltage during follow-up showed a rate of cardiovascular complications significantly lower than patients with increased or unchanged voltage magnitude.[20] The HOPE study enrolled patients with high cardiovascular risk (80% with chronic ischemic heart disease). During follow-up, those with persistent or newly-developed ECG criteria of LVH showed a significantly greater risk of complications (total and sudden death, heart failure, and stroke) than did patients with normalization of LVH criteria or a persistent normal ECG.[21] The LIFE study included >9000 hypertensives with ECG-defined LVH.[22] During follow-up, reduction of LVH criteria (Cornell

product voltage-duration and/or Sokolow-Lyon voltage) was accompanied by reduction in risk of cardiovascular complications. In contrast, increased criterion voltage magnitude was associated with a greater rate of cardiovascular complications. In fact, reduction of risk of stroke in patients treated with losartan[23] in this study may be due, at least to a good extent, to the greater cardioprotection afforded by the drug, manifested as greater regression of ECG-defined LVH rates[24] and lesser development of atrial fibrillation.[25] However, none of these studies describes the relationship between magnitude or severity of LVH voltage criteria and patient cardiovascular risk profile.

We show that a direct relationship exists between voltage magnitude criteria (Cornell, Sokolow-Lyon, or the combination of both) and cardiovascular risk profile of hypertensives included in the VIIDA study. Sokolow-Lyon criteria associated more with presence of myocardial infarction and patients in the highest quartile had higher BP and were more frequently men, although they were younger and had lower BMI. Cornell criteria associated more with heart failure and in the highest quartile we observed less BP control. The relationship between greater severity of LVH and greater prevalence of established cardiovascular disease in the 3 criteria used is of special interest.

These findings highlight the importance of conducting and correctly interpreting ECGs and using different LVH criteria to increase its detection. They also indicate the convenience of evaluating QRS complex voltage magnitude as this helps identify hypertensives with higher cardiovascular risk for whom we must be more rigorous about our control objectives, using therapies proven to have greater prognostic benefits. We also need to consider ECG voltage changes during follow-up. Voltage reduction is accompanied by more favorable prognosis,[20-22] whereas persistence of LVH or increased QRS complex voltage magnitude worsens prognosis, indicating the need to administer a more aggressive treatment or modify the therapeutic strategy.

The principal limitation of this study is its cross-sectional design with no follow-up of patients, which prevents us from definitively establishing the cause-effect relationship between LVH severity and prevalence of cardiovascular complications. As a result, we are unable to describe the duration of the associations found. Furthermore, a bias in selection may exist as a consequence of the possible selective survival of patients included in our study. Moreover, our conclusions apply to a population of hypertensives with high cardiovascular risk followed in cardiology clinics and we should be cautious when generalizing. We have limited our analysis to the 2 LVH criteria most widely used in clinical practice and do not know whether other criteria would produce the same results. Moreover, we have yet to define precisely the benefits of combining the 2 ECG criteria employed in this study. However, the study was performed under conditions of normal clinical practice, making this highly useful information which should be borne in mind in the evaluation and follow-up of these hypertense patients.

CONCLUSIONS

In this high cardiovascular risk population, attended in cardiology clinics, patients who meet Sokolow-Lyon or Cornell criteria present different profiles but both groups are at high cardiovascular risk. Consequently, we recommend employing the 2 criteria to increase detection of ECG-defined LVH and improve prognostic stratification of hypertensives. Moreover, we observed a relationship between LVH severity and prevalence of established cardiovascular disease which supports the use of ECG follow-up of these patients, in whom we should aim to achieve exhaustive BP control and eliminate LVH thru an energetic antihypertensive treatment including drugs of proven efficacy for this purpose.

ACKNOWLEDGEMENTS

The VIIDA study was designed and endorsed by the Hypertension and Outpatient Cardiology sections of the Spanish Society of Cardiology.

REFERENCES

1. Verdecchia P, Angeli F, Reboldi G, Carluccio E, Benemio G, Gattobigio R, et al. Improved cardiovascular risk stratification by a simple ECG index in hypertension. Am J Hypertens. 2003;16:646-52.
2. Levy D, Garrison RJ, Savage DD, Kannel WB, Castelli WP. Prognostic implications of echocardiographically determined left ventricular mass in the Framingham Heart Study. N Engl J Med. 1990;322:1561-6.
3. Schillaci G, Verdecchia P, Porcellati C, Cuccurullo O, Cosco C, Perticone F. Continuous relation between left ventricular mass and cardiovascular risk in essential hypertension. Hypertension. 2000;35:580-6.
4. Boden WE, Kleiger RE, Schechtman KB, Capone RJ, Schwartz DJ, Gibson RS. Clinical significance and prognostic importance of left ventricular hypertrophy in non-Q-wave acute myocardial infarction. Am J Cardiol. 1988;62:1000-4.
5. Ghali JK, Liao Y, Simmons B, Castaner A, Cao G, Cooper RS. The prognostic role of left ventricular hypertrophy in patients with or without coronary artery disease. Ann Intern Med. 1992;117:831-6.
6. Parfrey PS, Harnett JD, Griffiths SM, Taylor R, Hand J, King A, et al. The clinical course of left ventricular hypertrophy in dialysis patients. Nephron. 1990;55:114-20.
7. Verdecchia P, Porcellati C, Reboldi G, Gattobigio R, Borgioni C, Pearson TA, et al. Left ventricular hypertrophy as an independent predictor of acute cerebrovascular events in essential hypertension. Circulation. 2001;104:2039-44.
8. Verdecchia P, Reboldi G, Gattobigio R, Bentivoglio M, Borgioni C, Angeli F, et al. Atrial fibrillation in hypertension: predictors and outcome. Hypertension. 2003;41:218-23.
9. 2003 European Society of Hypertension-European Society of Cardiology guidelines for management of arterial hypertension. J Hypertens. 2003;21:1011-53.
10. 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;289:2560-72.
11. González-Juanatey JR, Mazon Ramos P, Soria Arcos F, Barrios Alonso V, Rodríguez Padial L, et al. Actualización (2003) de las guías de práctica clínica de la Sociedad Española de Cardiología en hipertensión. Rev Esp Cardiol. 2003;56:487-97.
12. Sokolow M, Lyon T. Ventricular complex in left ventricular hypertrophy as obtained by unipolar precordial and limb leads. Am Heart J. 1949;37:161-86.
13. Casale PN, Devereux RB, Alonso DR, Campo E, Kligfield P. Improved sex-specific criteria of left ventricular hypertrophy for clinical and computer interpretation of electrocardiograms: validation with autopsy findings. Circulation. 1987;75:565-72.
14. Rodríguez L. Usefulness of total-lead QRS voltage for determining the presence of left ventricular hypertrophy in systemic hypertension. Am J Cardiol. 1991;68:261-2.
15. Schillaci G, Verdecchia P, Borgioni C, Ciucci A, Guerrieri M, Zampi I et al. Improved electrocardiographic diagnosis of left ventricular hypertrophy. J Am J Cardiol. 1994;74:714-9.
16. Molloy TJ, Okin PM, Devereux RB, Kligfield P. Electrocardiographic detection of left ventricular hypertrophy by the simple QRS voltage-duration product. J Am Coll Cardiol. 1992;20:1180-6.
17. Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Dahlof B for the LIFE Study Investigators. Baseline characteristics in relation to electrocardiographic left ventricular hypertrophy in hypertensive patients: the Losartan intervention for endpoint reduction (LIFE) in hypertension study. The Life Study Investigators. Hypertension. 2000;36:766-73.
18. De Simone G, Devereux RB, Roman MJ, Alderman MH, Laragh JH. Relation of obesity and gender to left ventricular hypertrophy in normotensive and hypertensive adults. Hypertension. 1994;23: 600–6.
19. Bella JN, Devereux RB, Roman MJ, O'Grady MJ, Welty TK, Lee ET, et al. for the Strong Heart Study Investigators. Relations of left ventricular mass to fat-free and adipose body mass: the strong heart study. Circulation. 1998;98:2538-44.
20. Levy D, Salomon M, D'Agostino RB, Belanger AJ, Kannel WB. Prognostic implications of baseline electrocardiographic features and their serial changes in subjects with left ventricular hypertrophy. Circulation. 1994;90:1786-93.
21. Mathew J, Sleight P, Lonn E, Johnstone D, Pogue J, Yi Q, et al. Reduction of cardiovascular risk by regression of electrocardiographic markers of left ventricular hypertrophy by the angiotensin-converting enzyme inhibitor ramipril. Circulation. 2001;104: 1615-21.
22. Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Nieminen MS, et al. Regression of electrocardiographic left ventricular hypertrophy during antihypertensive treatment and the prediction of major cardiovascular events. JAMA. 2004;292:2343-9.
23. Dahlof B, Devereux RB, Kjeldsen SE, Julius S, Beevers G, De Faire U, et al. Cardiovascular morbidity and mortality in the Losartan Intervention for Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet. 2002;359: 995-1003.
24. Okin PM, Devereux RB, Jern S, Kjeldsen SE, Julius S, Nieminen MS, et al. Regression of electrocardiographic left ventricular hypertrophy by losartan versus atenolol: The Losartan Intervention for Endpoint reduction in Hypertension (LIFE) Study. Circulation. 2003;108:684-90.
25. Wachtell K, Lehto M, Gerdts E, Olsen MH, Hornestam B, Dahlof B, et al. Angiotensin II receptor blockade reduces new-onset atrial fibrillation and subsequent stroke compared to atenolol: the Losartan Intervention For End Point Reduction in Hypertension (LIFE) study. J Am Coll Cardiol. 2005;45:712-9.