Blood Pressure and Estimated Risk of Stroke in the Elderly Population of Spain
The PREV-ICTUS Study

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Background and Purpose—The objective of this study was to estimate the high blood pressure values and the 10-year risk of stroke in the Spanish general population aged 60 years or older using the Framingham scale.

Methods—This was a multicenter, population-based, cross-sectional study performed in Spanish primary care centers. A randomized selection of centers and recruitment population was used. We collected clinical, biochemical, and electrocardiographic data.

Results—We analyzed 7343 subjects (mean age, 71.6 years; standard deviation, 7.0; 53.4% females, 34.4% obese subjects, and 27.1% diabetic subjects). Electrocardiographic–left ventricle hypertrophy was present in 12.9% of the subjects, atrial fibrillation in 8.4%, and established cardiovascular disease in 28.9%; 73.0% already had hypertension diagnosed, and 12.8% showed high blood pressure without a prior diagnosis of hypertension. Among hypertensive subjects, 29.1% had high blood pressure on therapeutic objective, and of the total population 35.7% had high blood pressure under control. Those with hypertension already diagnosed showed a higher prevalence of other stroke risk factors (left ventricle hypertrophy, atrial fibrillation, diabetes, or established cardiovascular disease). The estimated 10-year stroke risk was 19.6% (standard deviation, 17.3%), and was greater in hypertensive patients (23.7%; standard deviation, 18.5) than in patients with high blood pressure without known hypertension (12.4%; standard deviation, 9.2), or in normotensive subjects (5.3%; standard deviation, 0.2; P<0.001).

Conclusion—The 10-year estimated stroke risk was 19.6%, and it was greater in hypertensive patients as compared with the remainder people at any blood pressure range. The concomitant stroke risk factors are more prevalent in patients with hypertension already diagnosed, which implies an important additional estimated risk of stroke. (Stroke. 2007;38:1167-1173.)

Key Words: blood pressure ■ elderly ■ hypertension ■ risk factors ■ stroke

Cardiovascular diseases constitute the first cause of death in the whole Spanish population. Both cerebrovascular disease and ischemic heart disease together account for 60% of global cardiovascular mortality.1 Although a decrease in stroke mortality has been observed in recent years,2 the number of hospital admissions attributable to this cause tends to increase. This is because of aging of the population, and because of increased survival among stroke patients.3

Age and high blood pressure (BP) are the most important risk factors for stroke. In the population setting, the relationship between BP and stroke risk is linear, and moreover begins to manifest at BP values considered to be within the normal range.4 In a meta-analysis of 61 follow-up studies, it was seen that from a systolic BP value of 115 mm Hg and a diastolic BP of 75 mm Hg, each additional 20-mm Hg increment in systolic BP and 10-mm Hg increment in diastolic BP doubles the stroke mortality rate in an age range of 40 to 89 years. The risk for each BP value, moreover, multiplies in each decade of life.4

The prevalence of arterial hypertension (HT) and BP treatment and control may therefore have a great impact on the incidence and mortality for stroke. In fact, a relationship has been observed at country level between HT prevalence and stroke mortality. In the United States and Canada, the prevalence of HT is lower, and the BP values are lower than in the European countries. This is in turn associated with lesser stroke mortality compared with the European countries, including Spain, one of the countries with the highest prevalence of HT and with the lowest rate of BP control among those included in the study.5 According to recent surveys,
45% among individuals aged 35 to 64 years and 68% in those aged 60 years or older, which implies ~10 million adults in Spain.

In our setting, to our knowledge, no studies to date have analyzed the estimated stroke risk in elderly subjects at population level, and data only exist in patients with HT. However, considering the relationship between BP and stroke mortality likewise at BP values below those defining HT, particularly among elderly people, we considered it of interest to conduct a general population-based study including subjects with BP values within the normal range. The main objective of the PREV-ICTUS study was to assess the BP distribution and to estimate the risk of stroke at 10 years in the Spanish general population aged 60 years or older.

**Patients and Methods**

The PREV-ICTUS study is an epidemiological, multicenter, cross-sectional, population-based study conducted in primary care centers throughout Spain by ~1200 physicians. This study was approved by an independent Clinical Research Ethics Committee. Between September and December 2005, each investigator recorded information on randomized patients.

**Selection of Study Participants**

The study included individuals aged 60 years or older who gave informed consent to participation. The exclusion criteria were the presence of serious concomitant diseases, or of disorders that, in the opinion of the investigator, could influence the collection of reliable information, and any mental or social condition that could complicate or prevent participation of the subject in the study.

Sample selection was based on calculation of the global sample size, with initial distribution by Spanish Autonomous Communities according to the population of individuals aged 60 years or older. Afterward, the same procedure was performed by provinces, an administrative division of each Autonomous Community. After distribution of the population by provinces, a randomized selection was made of primary care centers and consulting offices taking into account the population residency distribution in urban centers (>20 000 inhabitants), semi-urban areas (5000 to 20 000), and rural settings (<5000 inhabitants). The primary care center extraction procedure was performed based on public data sources of the different local health care services in each community. A randomized number was assigned to each center for center selection purposes with the development of specific software.

An investigator participated in each selected center, with randomized selection of 6 individuals aged 60 years or older, from the corresponding individualized health care cards. The selected individuals were invited by telephone to participate in the study. If the event contact could not be established or the subject refused to participate, the investigator could invite a replacement subject from a reserve randomized list. The percentage of replacements was 28%.

**Procedures**

Demographic data were collected along with anthropometric parameters, cardiovascular risk factors, and the presence of established cardiovascular diseases. Living habits, smoker status, alcohol consumption, and physical activity were recorded. Biochemical data were obtained from the clinical history (where available in the previous 6 months), or were requested from the laboratory at that time. Kidney function was estimated from the glomerular filtrate, calculated using the Modification of Diet in Renal Disease abbreviated equation. Systolic BP and diastolic BP were measured using an OMRON model M6 automated device. BP recordings were made twice, and were spaced 2 minutes apart taking the average of both values. The subjects were divided according to their current BP and previous diagnosis of HT as normotensive (BP not elevated and no previous diagnoses of HT), known hypertensive (subjects with HT previously diagnosed, whether their BP was controlled), and those with elevated BP but no previous diagnosis of HT. Values of BP <140/90 mm Hg for nondiabetic subjects and <130/80 mm Hg for diabetic subjects were considered controlled.

Electrocardiographic–left ventricle hypertrophy (LVH) was defined by the presence of at least one of the voltage criterion of Cornell or that of Sokolow. The presence of atrial fibrillation was also recorded.

Assessment of the risk of a first stroke at 10 years was based on the Framingham stroke risk scale, which includes the following variables: patient sex, age, systolic BP with or without antihypertensive treatment (mm Hg), diabetes mellitus, smoking, past or present cardiovascular disease, atrial fibrillation, and LVH as identified by ECG. This scale yields a score of between 1 and 30 points, corresponding by patient sex to a given estimated risk at 10 years.

**Statistical Analysis**

Sample size calculations used the latest population data presented by the Spanish National Statistics Institute in 2003: 42 717 064 inhabitants, of which 21.4% were 60 years old or older. For a confidence of 95% and an imprecision of 1%, a representative sample of these individuals would be 6468 inhabitants. The data obtained in relation to the distribution by autonomous communities and provinces were contrasted with the theoretical distribution derived from the initial population randomization conditions ($x^2$ all $\geq 0.861$).

Comparisons were made of the results among the different calculated risk groups. For simple bivariate group comparisons, use was made of the Student $t$ test for independent groups, or ANOVA in the case of intervention by some other categorical factors. A $\chi^2$ test was used to compare categorical variables. Binomial logistic regression analysis was used to determine the factors related to stroke risk.

**Results**

**General Characteristics of the Study Population**

A total of 7555 individuals were included in the study, of which 212 (2.8%) were excluded from the analysis because they failed to meet some inclusion criterion, or because the necessary basic information was lacking. The main characteristics of the 7343 subjects considered valid for the analysis stratified by sex are shown in Table 1; 27.7% came from the rural setting, 19.5% from semi-urban areas, and 52.7% from urban zones.

**Blood Pressure and Other Risk Factors for Stroke**

A total of 14.1% were normotensive, whereas 73.0% already had HT diagnosed, and 12.8% showed high BP without a previous diagnosis of HT. The mean BP was 143.4 (17.6)/80.7 (9.7) mm Hg. BP was higher among patients with high BP but no previous diagnosis of HT (150.0 [13.9]/82.9 [8.7] mm Hg) versus known hypertensive subjects (145.7 [17.6]/81.5 [9.8] mm Hg) and the normotensive (126.5 [8.7]/74.7 [7.2] mm Hg) ($P<0.001$ for all comparisons).

In the whole population, 35.7% of the subjects presented controlled BP values, <140/90 mm Hg in 44.0% of the nondiabetic subjects, and <130/80 mm Hg in 13.3% of the subjects with diabetes mellitus. Systolic BP was below the therapeutic control objective in 37.7% of cases, whereas diastolic BP was below the objective in 71.6% ($P<0.001$). Considering only the patients with HT diagnosed, therapeutic control was seen to have been achieved in 29.1% of the patients. A larger proportion of women were below the therapeutic control objective (36.9% versus 34.3%; $P=0.021$).
Table 2 reports the characteristics of the normotensive patients, subjects with known HT, and patients with elevated BP but no previous diagnosis of HT. Compared with the patients without diagnosed HT, those with HT diagnosed were slightly older, with a slightly lower percentage of smokers and a higher prevalence of diabetes mellitus, atrial fibrillation, LVH, and established cardiovascular disease ($P<0.001$).

### 10-Year Risk for a First Stroke

Risk was estimated in the 6304 patients, in the absence of any previous stroke, for whom all the necessary information was available. The mean 10-year estimated risk for a first stroke for the global sample was 19.6% (standard deviation [SD], 17.3%), and was greater in males (21.4%; SD, 16.5) than in females (18.0%; SD, 17.9; $P<0.001$); 37.3% had a risk $\geq 20\%$. The estimated stroke risk was greater in patients with HT previously diagnosed (23.7%; SD, 18.5) than in patients with high BP but no previous diagnosis of HT (12.4%; SD, 9.2), and was lower in normotensive subjects (5.3%; SD, 0.2; $P<0.001$). Figure 1 shows the estimated risk at 10 years in the aforementioned groups of subjects stratified by sex. In all 3 categories, the estimated risk was greater in men than in women.

Figure 2A and 2B show the estimated stroke risk stratified by BP values and by the diagnosis or nondiagnosis of HT in males and females. In each BP interval, the estimated risk of stroke was greater in patients previously diagnosed with HT than in patients with high BP but no previous diagnosis of HT, or in the normotensive subjects ($P<0.001$ for all comparisons).

To evaluate the specific impact of each variable on the estimation of stroke risk in the study population, a multivariate model was constructed including the variables reflected in the stroke risk calculation table, and to which sex, diastolic BP, body mass index, cholesterol concentration, and BP

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**TABLE 1. Descriptive Data Corresponding to 7343 Subjects Included in the PREV-ICTUS Study**

<table>
<thead>
<tr>
<th></th>
<th>Males (n=3422)</th>
<th>Females (n=3912)</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years*</td>
<td>71.6 (SD 7.0)</td>
<td>72.2 (SD 7.1)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Body mass index, kg/m²*</td>
<td>28.4 (SD 3.8)</td>
<td>29.1 (SD 4.8)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Abdominal circumference, cm*</td>
<td>101.3 (SD 12.6)</td>
<td>97.0 (14.1)</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg*</td>
<td>143.5 (17.5)</td>
<td>143.4 (17.4)</td>
<td>0.778</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg*</td>
<td>80.7 (9.7)</td>
<td>80.7 (9.6)</td>
<td>0.771</td>
</tr>
<tr>
<td>Blood pressure categories</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normotension</td>
<td>43.2%</td>
<td>56.8%</td>
<td>0.024</td>
</tr>
<tr>
<td>High blood pressure, no diagnosis of hypertension</td>
<td>46.8%</td>
<td>53.4%</td>
<td></td>
</tr>
<tr>
<td>Known hypertension</td>
<td>49.3%</td>
<td>50.7%</td>
<td></td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$&lt;25.0$</td>
<td>16.9%</td>
<td>19.5%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>53.1%</td>
<td>42.1%</td>
<td></td>
</tr>
<tr>
<td>$&gt;29.9$</td>
<td>30.0%</td>
<td>38.4%</td>
<td></td>
</tr>
<tr>
<td>Increased abdominal circumference†</td>
<td>44.8%</td>
<td>73.6%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Sedentary</td>
<td>49.3%</td>
<td>57.5%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active smoker</td>
<td>18.6%</td>
<td>2.9%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>50.4%</td>
<td>5.0%</td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>31.0%</td>
<td>92.1%</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>38.3%</td>
<td>85.5%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Mild</td>
<td>45.7%</td>
<td>13.2%</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>14.8%</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>1.3%</td>
<td>0.1%</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26.3%</td>
<td>27.9%</td>
<td>0.002</td>
</tr>
<tr>
<td>Blood pressure in therapeutic goal‡</td>
<td>34.3%</td>
<td>36.9%</td>
<td>0.021</td>
</tr>
<tr>
<td>Left ventricle hypertrophy</td>
<td>14.3%</td>
<td>11.7%</td>
<td>0.001</td>
</tr>
<tr>
<td>Glomerular filtration rate $&lt;60$ mL/min per 1.73 m²</td>
<td>13.9%</td>
<td>36.0%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>History of cardiovascular disease</td>
<td>34.9%</td>
<td>23.6%</td>
<td>$&lt;0.001$</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>8.9%</td>
<td>7.9%</td>
<td>0.137</td>
</tr>
</tbody>
</table>

*Expressed as mean (SD).
†Abdominal circumference $>102$ (males) or $>88$ cm (females).
‡$<140/90$ mm Hg in nondiabetic subjects or $<130/80$ mm Hg in diabetic subjects.
BMI indicates body mass index.
control were added. In the resulting model, the greatest impact as stroke risk factor corresponded to atrial fibrillation, followed by patient age and LVH (Table 3).

### Discussion

In this population-based study, performed in Spanish population aged 60 years or older, the estimated risk of stroke at 10 years was 19.6%, and was greater among the subjects with HT diagnosed than in either the normotensive subjects or those with high BP but no previous diagnosis of HT. Because stroke risk factors were more prevalent among patients with HT diagnosed, that implied, for one same BP level, an additional risk of stroke in those with HT diagnosed compared with the subjects without diagnosed HT.

We included the population aged 60 years or older in our study because these subjects concentrate the greatest stroke risk levels. Our randomized population totaled 9,156,594 inhabitants, equivalent to 21.4% of the global Spanish population in 2003. In the coming years, an important increase in the number of elderly people is expected in our setting.

This situation can pose enormous health and economic problems for the Spanish health care system.

Subject selection has been based on randomization from individualized health care cards. Whereas the sample resulting from such stratified selection is not strictly population-based, it comes very close to this setting, because in Spain health care card distribution is universal and without limitations in terms of access. It is estimated that the proportion of the population not covered by the card system is <5% of the global population of Spain, with this being considered a negligible figure. The study population was adjusted to the number and distribution to the theoretical sample size obtained from the population census by age, autonomous community, sex, and residency setting (rural, semi-urban, and urban).

The prevalence of diagnosed HT was 73.0%, which is very similar to the 68.3% recorded in another population-based study in Spain; likewise in a population aged 60 years or older. An additional 12.8% moreover presented BP values above the limits considered normal. However, these patients presented a lesser prevalence of LVH and other risk factors;
consequently, they probably represent individuals with only occasional BP elevations, or with recent-onset HT not previously diagnosed. This implies a high percentage of diagnosis of HT at these ages, and a lesser proportion of patients who are unaware of their HT than in the study published by Banegas et al., because in the period between 1990 and 2001, an increase from 52% to 65% had been recorded in the awareness of HT. Nevertheless, BP control remains deficient. Only 35.7% of the subjects presented BP values within the normal range. When only considering the patients with HT diagnosed, this figure further decreases to 29.1%. The recorded BP control values are similar to those found in other European countries.

The estimated 10-year stroke risk in this population was 19.6%, and was greater in patients with HT diagnosed than in patients with elevated BP but not HT previously diagnosed, or in normotensive subjects. The relationship between HT and stroke is well-known at population level. In a study conducted in the United States, Canada, and 6 European countries, the prevalence of HT was seen to be higher in Europe than in either the United States or Canada, in the same way as stroke mortality. The relationship between BP and mortality caused by stroke is already apparent in BP ranges currently considered to be normal, and persists at all adult ages. BP reduction has been shown to be effective in lowering stroke risk in both primary and secondary prevention.

In our study, the estimated risk of stroke at 10 years was lower in patients with elevated BP without diagnosis of HT than in patients with HT previously diagnosed despite slightly higher BP values in the patients without a diagnosis of HT. On stratifying by BP levels according to the classification of the Seventh Report of the Joint National Committee, estimated risk was seen to be greater among the patients with a
TABLE 3. Multiple Linear Regression Model

<table>
<thead>
<tr>
<th></th>
<th>Nonstandardized Coefficients</th>
<th>Standardized Coefficient</th>
<th>t</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Standard Error</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>24.890</td>
<td>0.357</td>
<td>0.401</td>
<td>69.653</td>
</tr>
<tr>
<td>Left ventricle hypertrophy</td>
<td>18.830</td>
<td>0.302</td>
<td>0.328</td>
<td>62.353</td>
</tr>
<tr>
<td>Age</td>
<td>0.902</td>
<td>0.013</td>
<td>0.352</td>
<td>68.721</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.247</td>
<td>0.007</td>
<td>0.235</td>
<td>33.963</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>8.609</td>
<td>0.225</td>
<td>0.205</td>
<td>38.339</td>
</tr>
<tr>
<td>Established cardiovascular disease</td>
<td>9.310</td>
<td>0.257</td>
<td>0.217</td>
<td>36.283</td>
</tr>
<tr>
<td>Blood pressure control</td>
<td>-0.624</td>
<td>0.276</td>
<td>-0.016</td>
<td>-2.263</td>
</tr>
</tbody>
</table>

Factors of greatest impact on estimated stroke risk at 10 years. F=5192.135; 7 degrees of freedom. P=0.000.

R²=89.8%. Durbin-Watson: h=1.934.

Sex, diastolic BP, body mass index, and cholesterol concentration were included in the model.

In the multiple linear regression model, patient age, atrial fibrillation, and LVH were factors of considerable impact on risk estimation in this population in the multivariate analysis. In this model, however, systolic BP had a lower impact than age, atrial fibrillation, or LVH. This finding is conditioned by the subjects without known HT, who showed high BP but a low prevalence of LVH and of atrial fibrillation, and consequently in whom the estimated risk of stroke were lower. Nevertheless, HT, because of its greater prevalence, should remain as the most important modifiable risk factor for stroke.

The high prevalence of DM and electrocardiographic LVH have already been reported in earlier studies of hypertensive patients with ages similar to those of our own subjects.8,9 The presence of LVH on the electrocardiograph or evidenced at echocardiography is associated with an increased risk of stroke in hypertensive patients,28 as well as atrial fibrillation.29 Diabetes is a well-known cardiovascular risk factor that is also associated with an increased risk of stroke30 and an excess of stroke mortality in both sexes.31 The grouping of cardiovascular risk factors in this population conditions a higher estimated risk of stroke. Consequently, reduction in cardiovascular risk in patients with HT requires not only BP control but also maximum protection of the HT target organs.

In the LIFE study, LVH regression as evidenced on the electrocardiograph according to both the Sokolow-Lyon voltage and Cornell product criteria was associated with a greater reduction in the incidence of stroke during a follow-up period of ≈ 5 years.32

The limitations of the present study came from the use of equations to estimate cardiovascular risk. Although some scales are available, the Framingham Stroke Profile, which uses a Cox proportional risk model, is the most widely used. This scale even updated for being used in patients with treated HT and in patients with new-onset atrial fibrillation33,34 does not consider the potential impact of other documented risk factors that contribute to the stroke risk estimation. One of its limitations is the fact that the Framingham scale has not been tested as a tool to improve the efficiency of the prevention programs. Additionally, this scale has not been calibrated for our population. In earlier studies by our group,8,9 however, the estimation afforded by the Framingham scale proved congruent with the stroke mortality data recorded in this country.

Nevertheless, the present study is of value, because it has been conducted in a large and representative sample of the elderly Spanish population in its usual health care setting, and was randomly selected with a proportional distribution among autonomous communities and health care setting.

In summary, the prevalence of HT in patients aged 60 years or older is very high. The estimated stroke risk at 10 years in this population is 19.6%, and is conditioned by patient age and BP, as well as by coadjuvant factors (LVH, atrial fibrillation, diabetes mellitus, or established cardiovascular disease). These latter factors are more common in patients who have a known history of HT, and suppose an important added estimated risk of stroke. The population with high BP in the absence of a previous diagnosis of HT presents a lesser estimated risk of stroke, because of the lesser prevalence of other risk factors. The control of BP and of other cardiovascular risk factors may have an important impact on the reduction of stroke risk. Identification of the factors that condition such risk may help to define preventive measures targeted to the population to improve BP control and reduce the impact on target organs.

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Disclosures

None.

References


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