Differences in Blood Pressure Control and Stroke Mortality Across Spain

The Prevención de Riesgo de Ictus (PREV-ICTUS) Study

Josep Redón, Luis Cea-Calvo, José V. Lozano, Juan C. Martí-Canales, José L. Llisterrri, Jose Aznar, Jorge González-Esteban, on behalf of the investigators of the PREV-ICTUS Study

Abstract—The objective was to assess the stroke risk and prevalence of the cardiovascular risk factors and to analyze their relationship with the specific stroke rates of mortality in each of the autonomic communities of Spain. We conducted a multicenter, cross-sectional study of population >60 years old in Spanish primary care centers. In all of the subjects, clinical, biochemical, and electrocardiographic data were obtained, and the 10-year stroke risk was calculated using the Framingham score. Mortality rates of stroke, age and sex adjusted, were obtained for each of the autonomic communities from the Ministry of Health. A total of 7343 subjects (mean age: 71.6 years, 53.4% women, 34.4% obese, and 27.1% diabetic subjects) were analyzed. A total of 73% were already diagnosed with hypertension. Among hypertensive subjects, 29.1% had blood pressure on therapeutic objective, and, of the total population, 35.7% had blood pressure under control. ECG–left ventricular hypertrophy was present in 12.9% of the subjects. The estimated stroke risk was 19.6%. Stroke mortality rates were significantly related to the estimated 10-year stroke risk ($r=0.41$; $P<0.05$) in each autonomic community. Poor hypertension control ($P=-0.42$; $P<0.05$) and prevalence of ECG–left ventricular hypertrophy ($P=0.52$; $P<0.05$) were the main factors related to the stroke mortality rates after controlling by age, sex, obesity, diabetes, and urban setting. Differences in stroke mortality throughout the autonomic communities of Spain were associated with indexes of worse blood pressure handling, low control rates, and high left-ventricular hypertrophy.

Key Words: hypertension ■ blood pressure ■ stroke ■ elderly ■ risk factors ■ stroke mortality ■ autonomic communities of Spain

Stroke remains a major healthcare problem for which age and hypertension (HT) are the factors with the largest impact. Although age, which doubles the risk for each successive decade after age 55 years, is a nonmodifiable factor, HT is the most important one susceptible of intervention. The relationship between blood pressure (BP) values and the risk of cerebrovascular events has been consistently established in multiple populations, and antihypertensive treatment has been demonstrated to reduce the risk in as much as 48% for 6 mm Hg of BP reduction. Despite the advances in antihypertensive treatment, stroke is still one of the most common HT-induced cardiovascular diseases. In a systematic analysis of outcome trials for antihypertensive treatment, >50% of the events were stroke. Both the prevalence of HT and the rate of controlled patients have been related to the rate of stroke mortality in the United States and Canada, as well as in several European Countries among which Spain was 1 of those included in the report.

Rates of stroke mortality in Spain, however, differ largely among different parts of the country. Taking advantage of the administrative division of Spain, which includes 17 autonomic communities (CCAs), specific mortality rates for each of them have been reported annually. According to the last released data, for 2002 the highest mortality rate for stroke adjusted for age and sex accounted for 99 per 100 000 inhabitants per year in 1 CCAA and the lowest accounted for 44 per 100 000 inhabitants. In between, there were the rates for the other 15 CCAAs. Potential explanations for these differences in the mortality rates for stroke have been the motive of controversy among epidemiologists, but the real reasons are still unclear, because no study went in deep to answer the question.

The Prevención de Riego de Ictus (PREV-ICTUS) Study is a community-based study designed to assess the risk of stroke in the general population of Spain >60 years old. The population of the study, which included >7000 people, was...
TABLE 1. General Characteristics of the Study Population

<table>
<thead>
<tr>
<th>CCAA</th>
<th>No. of Investigators</th>
<th>No. of Subjects</th>
<th>Rate of Replacements (%)</th>
<th>Age (y)</th>
<th>Women (%)</th>
<th>BMI (kg/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Andalucia</td>
<td>225</td>
<td>1145</td>
<td>32</td>
<td>70.9(70.5 to 71.3)</td>
<td>51.9(49.0 to 54.8)</td>
<td>29.3(29.0 to 29.6)</td>
</tr>
<tr>
<td>Aragon</td>
<td>44</td>
<td>258</td>
<td>30</td>
<td>72.2(71.3 to 73.0)</td>
<td>51.8(45.6 to 57.9)</td>
<td>28.3(27.8 to 28.8)</td>
</tr>
<tr>
<td>Asturias</td>
<td>40</td>
<td>235</td>
<td>24</td>
<td>71.9(71.0 to 72.9)</td>
<td>54.5(48.1 to 60.8)</td>
<td>28.6(28.1 to 29.2)</td>
</tr>
<tr>
<td>Baleares</td>
<td>24</td>
<td>145</td>
<td>25</td>
<td>71.1(69.9 to 72.3)</td>
<td>46.9(38.8 to 55.0)</td>
<td>29(28.2 to 29.7)</td>
</tr>
<tr>
<td>Canarias</td>
<td>37</td>
<td>215</td>
<td>28</td>
<td>71.6(70.6 to 72.6)</td>
<td>59.1(52.5 to 65.6)</td>
<td>29.9(29.2 to 30.6)</td>
</tr>
<tr>
<td>Cantabria</td>
<td>18</td>
<td>104</td>
<td>33</td>
<td>72(70.6 to 73.5)</td>
<td>50(40.4 to 59.6)</td>
<td>27.9(27.1 to 28.8)</td>
</tr>
<tr>
<td>Castilla Leon</td>
<td>93</td>
<td>562</td>
<td>35</td>
<td>72.9(72.3 to 73.4)</td>
<td>55.4(51.3 to 59.5)</td>
<td>28.6(28.2 to 28.9)</td>
</tr>
<tr>
<td>Castilla la Mancha</td>
<td>55</td>
<td>333</td>
<td>21</td>
<td>73.6(72.8 to 74.4)</td>
<td>53.9(48.6 to 59.3)</td>
<td>29.5(29.0 to 30.0)</td>
</tr>
<tr>
<td>Cataluña</td>
<td>201</td>
<td>1189</td>
<td>24</td>
<td>71.8(71.4 to 72.2)</td>
<td>52.9(50.0 to 55.7)</td>
<td>28.3(28.0 to 28.5)</td>
</tr>
<tr>
<td>Extremadura</td>
<td>36</td>
<td>222</td>
<td>27</td>
<td>71.2(70.3 to 72.1)</td>
<td>51.8(45.2 to 58.4)</td>
<td>29.5(28.8 to 30.1)</td>
</tr>
<tr>
<td>Galicia</td>
<td>100</td>
<td>602</td>
<td>26</td>
<td>72.5(71.9 to 73.1)</td>
<td>54.2(50.3 to 58.2)</td>
<td>28.7(28.3 to 29.1)</td>
</tr>
<tr>
<td>Madrid</td>
<td>149</td>
<td>855</td>
<td>23</td>
<td>71.5(71.0 to 72.0)</td>
<td>55.9(52.6 to 59.3)</td>
<td>28.9(28.6 to 29.2)</td>
</tr>
<tr>
<td>Murcia</td>
<td>28</td>
<td>170</td>
<td>31</td>
<td>71.8(70.8 to 72.9)</td>
<td>48.8(41.3 to 56.3)</td>
<td>28.9(28.2 to 29.6)</td>
</tr>
<tr>
<td>Navarra</td>
<td>18</td>
<td>96</td>
<td>30</td>
<td>73.1(71.6 to 74.6)</td>
<td>59.4(49.6 to 69.2)</td>
<td>28.8(27.9 to 29.7)</td>
</tr>
<tr>
<td>La Rioja</td>
<td>10</td>
<td>54</td>
<td>28</td>
<td>72.9(71.2 to 74.6)</td>
<td>46.3(33.9 to 59.6)</td>
<td>28.4(26.9 to 29.9)</td>
</tr>
<tr>
<td>País Vasco</td>
<td>66</td>
<td>391</td>
<td>34</td>
<td>72.2(71.5 to 72.9)</td>
<td>50.1(45.2 to 55.1)</td>
<td>28.3(27.8 to 28.7)</td>
</tr>
<tr>
<td>Comunidad Valenciana</td>
<td>129</td>
<td>767</td>
<td>22</td>
<td>71.9(71.4 to 72.4)</td>
<td>54.5(51.0 to 58.1)</td>
<td>28.7(28.4 to 29.1)</td>
</tr>
<tr>
<td>Total of Spain</td>
<td>1273</td>
<td>7343</td>
<td>28</td>
<td>71.9(71.7 to 72.1)</td>
<td>53.4(52.3 to 54.5)</td>
<td>28.8(28.7 to 28.9)</td>
</tr>
</tbody>
</table>

Values are average and 95% CI.

stratified not only according to age, sex, and urban distribution but also according to the population of the CCAAs, allowing us to analyze separately each of the CCAAs. Therefore, the objective of the present study was to assess the stroke risk, as well as the prevalence of the cardiovascular risk factors in each of the CCAAs and to analyze the relationship with the specific stroke rates of mortality.

Methods

The PREV-ICTUS Study is an epidemiological, multicenter, cross-sectional and 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 6 randomly assigned patients who were included in the study after obtaining written informed consent. The primary objective of the study was to estimate the 10-year risk of stroke in the Spanish general population aged ≥60 years, using the Framingham scale.10,11

Selection of Participating Subjects

The study included individuals aged ≥60 years who gave informed consent to participate. 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 CCAAs according to the population of individuals aged ≥60 years found in each CCAA. Afterward, the same procedure was carried out by provinces, administrative divisions of each CCAA. After distribution of the population by provinces, a randomized selection was made of primary care centers and consulting offices to reach the sample corresponding to each province, moreover, taking into account the population residency distribution in urban centers (>20 000 inhabitants), semirural areas (5000 to 20 000), and rural settings (under 5000 inhabitants). The primary care center extraction procedure was carried out based on public data sources of the different local health care services in each CCAA. A randomized number was assigned to each center for center selection purposes. This number was obtained using Visual Basic (“Rnd” and “Randomize”), with the development of specific software.

An investigator participated in each selected center, with randomized selection of 6 individuals aged ≥60 years, from the corresponding individualized healthcare 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

After inclusion of the individuals in the study, data collection was carried out in a structured manner that was explained previously.10 Briefly, BP values were measured using an OMRON model M6 automated device.12 The subjects were divided according to their current BP and previous diagnosis of HT as normotensive patients (BP not elevated and no previous diagnoses of HT), known hypertensive subjects (subjects with a previous diagnoses of HT, whether their BP was controlled or not), and patients 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 on control.

ECG was made to assess left ventricular hypertrophy (LVH). LVH was defined by the presence of ≥1 of the 2 following criteria: the voltage criterion of Casale et al13 and that of Sokolow and Lyon.14 Assessment of the 10-year risk of a first stroke was based on the Framingham risk scale.11 This scale includes the following variables: patient sex, age, SBP with or without antihypertensive treatment (millimeters of Mercury), 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 to a given estimated risk at 10 years.10 Risk score was calculated for each individual and then averaged for the CCAA.

Specific mortality rate for each CCAA was obtained for the yearly report published in the official Web site of the Health Ministry of
Student

For simple bivariate group comparisons, use was made of the characteristics. Concomitant diseases and patient sex were also considered. Percentages and 95% CI. Comparisons were made of the results whereas qualitative variables were described as frequencies or distribution among the CCAAs, differences for body mass index, prevalence of obesity, and rate of smokers were observed.

### Statistical Analysis

Sample size was powered to be representative of the Spanish population and each of the CCAAs for >60 years. For calculation, use was made of the latest population data presented by the Spanish National Statistics Institute in 2003, where the Spanish population census totaled 42 717 064 inhabitants, of which 9 156 594 were aged 60 years. For calculation, the Student t test for independent groups, or ANOVA in the case of intervention by some other categorical factor. Bonferroni correction was applied for multiple comparisons. A goodness-of-fit test. Quantitative variables were expressed as the mean and 95% CI, whereas qualitative variables were described as frequencies or percentages and 95% CI. Comparisons were made of the results among the different CCAAs and relating the latter to other characteristics. Concomitant diseases and patient sex were also considered. For simple bivariate group comparisons, use was made of the Student’s goodness-of-fit test. Quantitative variables were expressed as the mean and 95% CI, whereas qualitative variables were described as frequencies or percentages and 95% CI. Comparisons were made of the results among the different CCAAs and relating the latter to other characteristics. Concomitant diseases and patient sex were also considered. For simple bivariate group comparisons, use was made of the Student’s t test for independent groups, or ANOVA in the case of intervention by some other categorical factor. Bonferroni correction was applied for multiple comparisons. A goodness-of-fit test was used to compare categorical variables. Lastly, the relationships between variables of each CCAA with their specific mortality rates, adjusted by age and sex, were assessed by using Pearson’s correlation coefficient and multiple regression analysis.

### 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 data relating to the final sample distributed by CCAAs and provinces were fitted to the calculated population distribution (the least value of significance recorded being 0.861), along with the age, sex, and residency setting distribution.

The general characteristics of the study population for each CCAA are shown in Table 1. Although no statistically significant differences were observed for age and sex distribution among the CCAAs, differences for body mass index, prevalence of obesity, and rate of smokers were observed.

#### Prevalence of Risk Factors

Differences in the prevalence of the risk factors analyzed were seen among the CCAAs. Overall in Spain, 73.0% were already diagnosed with HT, and 12.8% showed high BP without a previous diagnosis of HT. These rates differed largely among the CCAAs, ranging from 55.6% to 79.4%, Table 2. Taking as a reference the CCAA with the highest prevalence of HT, 5 CCAAs showed significantly lower prevalences. Considering only the patients diagnosed with HT, BP control was observed in 29.1%, ranging from 22.2% to 40.6% in the different CCAAs, whereas the rate of BP below the predefined thresholds in the population was 35.7%, ranging from 28.5% to 45.4%. The highest prevalence of ECG-LVH in 1 CCAA was 19.6%, a percentage significantly higher that in the other 10 CCAAs (Table 2). Considering the other risk factors, prevalence of obesity and diabetes also differed among the CCAAs (Table 1).

#### Estimation of the 10-Year Risk for a First Stroke

The mean 10-year estimated risk for a first stroke for the global sample was 19.6% (SD: ±17.3%). In turn, 12.7% presented an estimated risk of ≥5%, whereas 50.0% showed a risk of 6% to 20%, and 37.3% had a risk of ≥20%. The highest calculated stroke risk was 24.3% in 1 CCAA, and the lowest was 18.0%, the rest of them showing calculated risks...
between those figures. The CCAA with the highest risk had a figure significantly higher than the other 7 CCAAs (Table 1).

**Risk Factors, Global Stroke Risk, and Stroke Mortality**

The stroke mortality rates for each of the CCAA plotted against the estimated stroke risk are shown in Figure 1. A positive and significant relationship between mortality rate and the calculated stroke risk was observed ($r=0.41$; $P<0.05$) for the CCAAs. Likewise, the mortality rate was significantly and inversely related to the rate of BP control, the rate of BP below the thresholds in the population, and the prevalence of ECG-LVH. The association was independent of other characteristics of the study population, such as the prevalence of LVH. The association was independent of other characteristics of the study population, such as the prevalence of obesity ($r=-0.42$; $P<0.05$) or in the total population ($r=-0.61$; $P>0.01$), as well as positively related to the prevalence of LVH ($r=0.53$; $P<0.05$; Figure 1). No correlation was observed for age ($r=0.21$; $P=0.41$), prevalence of obesity ($r=0.13$; $P=0.63$), diabetes ($r=0.26$; $P=0.31$), or atrial fibrillation ($r=0.15$; $P=0.56$).

A multivariate regression analysis was used to analyze the factors independently related to the stroke mortality in the CCAAs. Both the rate of BP on therapeutic goal among hypertensive subjects and the prevalence of LVH remained as the independent factors related to the mortality rate, accounting for 62% of the variance. In a stepwise model, the rate of BP control accounted for 36% and the LVH accounted for 24% of the variance (Table 3). The graphic representation of the multiple regression analysis is in Figure 2.

**Discussion**

The present population-based study, which estimates stroke risk in the population of CCAAs of Spain aged ≥60 years, unraveled the potential reason for the different stroke mortality rates in the different CCAAs of Spain. Mortality rates for stroke, which were related to the estimated stroke risk by using the Framingham score, were independently associated with the rate of BP control, the rate of BP below the thresholds in the population, and the prevalence of ECG-LVH. The association was independent of other characteristics of the study population, such as the prevalence of diabetes, obesity, atrial fibrillation, or urban distribution.

The study has to be interpreted within the context of its limitations and strengths. The present was an ecological study that explored possible relationships between health statistics and population characteristics, stroke mortality rates, and prevalence of cardiovascular risk factors. Although inferences from associations observed in an ecological study may not necessarily pertain to the individuals within the group, especially when outcomes from long-term exposures were studied, they help to develop hypotheses to further evaluation with analytical studies, and they have a distinct advantage because of their statistical power to detect small risks. Estimates may be subject to ecological bias, but neither theoretical nor empirical analysis has offered consistent guidelines for the interpretation of ecological analysis.
Nevertheless, the present study is of value, because it has been conducted in a large and representative sample of the elderly Spanish population at the usual healthcare setting and randomized with a proportional distribution among CCAAs and the healthcare setting. Because the study was conducted with a unified health system within a single country, the data are more likely to be comparable among sites than might be expected in cross-cultural studies. The number, characteristics, and selection of the study population were appropriate to minimize the potential bias and to analyze the purposed

Figure 1. Relationship between stroke risk (A), percentage of BP control among the hypertensive subjects (B), percentage of BP in the population (C), percentage of ECG-LVH (D), and stroke mortality per 10^5 inhabitants adjusted by age and sex in the CCAA.

| TABLE 3. Factors Associated With Stroke Mortality by Using Multiple Regression Analysis |
|---|---|---|---|---|
| Independent Variables | β | SD | P | R2 |
| First step | | | | |
| ECG to LVH (%) | 1.653 | 0.704 | 0.029 | 0.23 |
| Second step | | | | |
| ECG to LVH (%) | 2.204 | 0.551 | 0.001 | |
| BP controlled among HT subjects (%) | 1.255 | 0.376 | 0.004 | 0.55 |
| First step | | | | |
| BP controlled in the general population (%) | 1.388 | 0.493 | 0.016 | 0.34 |
| Second step | | | | |
| BP controlled in the general population (%) | 1.332 | 0.405 | 0.007 | |
| ECG to LVH (%) | 1.543 | 0.559 | 0.018 | 0.59 |

Diabetes, atrial fibrillation, obesity, and the precision of estimates within each CCAA were forced in the model and were not significant.
objective. We included the population aged ≥60 years, because these subjects concentrate the greatest cardiovascular and stroke risk levels. Our randomly assigned population totaled 9,156,594 inhabitants, equivalent to 21.4% of the global Spanish population in 2003 according to the National Statistics Institute. Subject selection has been based on randomization from primary care centers, physicians, and individualized health care cards. Although the sample resulting from such stratified selection is not strictly population based, it comes very close to this setting, because in Spain, healthcare 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, 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, semiurban, and urban).

Subjects’ characteristics were obtained during a structured interview, and risk of stroke was calculated by using the Framingham score. The scales for assessing risk of stroke have some limitations. Mainly, they do not consider the potential impact of recently documented risk factors that contribute to the stroke risk estimation. Furthermore, the scale has not been tested as a tool to improve the efficiency of the prevention programs. In the present study, an additional limitation is that the scale has developed in the Framingham population, and it has not been validated in the population of Spain. Nevertheless, the significant relationship observed between the scores yielded by the using the scale for each CCAA and its mortality rate in the present study supports in part the clinical use in our setting.

Additional limitations of the study are that results obtained can only be applied to the population aged ≥60 years and that the cross-sectional design only allowed us to calculate prevalence and stroke risk at the time of the study. This may vary over time if vigorous treatment measures are adopted.

Adjusting for potential confounding variables, the control rate of HT among hypertensive subjects, the control rate of BP in the population, and the prevalence of ECG-LVH were independently related to the figure of mortality in the CCAAs. HT control rate was 1 of the 2 main factors associated with stroke mortality: the lower the control the higher the risk. The prevalence of diagnosed HT was 73.0%, which was very similar to the 68.3% recorded in another population-based study in Spain, also in a population aged ≥60 years. Moreover, an additional 12.8% presented BP values above the limits considered normal. When the percentage of the BP under control in the total population, which accounted for those with BP <140/90 mm Hg or <130/80 mm Hg in the case of diabetes or previous cardiovascular event, was considered, a strong relationship with the mortality rate emerged. The observed relationship between BP control rates and mortality was in agreement with the knowledge about BP and stroke. These data were also congruent with the data published by Wolf-Maier et al in which the stroke mortality in countries on the 2 side of the Atlantic was compared. A direct relationship between stroke mortality rates and the prevalence and control rates of HT was demonstrated. We have observed the same relationship even inside the same country.

Prevalence of LVH is the other risk factor that explains the differences in mortality among CCAAs. LVH is highly dependent not only on the severity of BP elevation but also on the time duration of HT and the predisposition to develop HT-induced organ damage; consequently, it offers additional information to that provided by the BP values. The presence of LVH on the ECG or evidenced at echocardiography, as well as atrial fibrillation, is associated with an increased risk of stroke in hypertensive patients. Consequently, reduction in cardiovascular risk in hypertensive patients requires not only BP control but also maximum protection of the HT target organs. In the Losartan Intervention For Endpoint (LIFE) Study, LVH regression, as evidenced in the ECG according to both the Casale et al and Sokolow and Lyon product criteria, was associated with a greater reduction in the incidence of stroke during a follow-up period of approximately 5 years.

Reasons for these significant differences in BP control and in the prevalence of LVH among the CCAAs are not well understood, and the underlying causes are unknown. Only genetic, as well as racial, factors can be excluded, because all of the subjects were whites of European origin, and no great migratory fluxes occurred in the past. Differences in dietary habits, cultural level, and use of antihypertensive medication among the different parts of Spain can contribute to the observed differences in HT control rates, although the impact...
of each of them will be difficult to accomplish. Prevalence of other stroke risks (diabetes, obesity, atrial fibrillation, and residence setting) that was included in the present analysis was not associated with the mortality risk. The potential contribution of other potential factors not tested, however, cannot be excluded.

In the coming years, an important increase in the number of elderly people is expected in our setting. Thus, the percentage of individuals aged ≥60 years in this country is expected to grow by 23% by the year 2026. This situation can pose enormous health and economic problems for the Spanish healthcare system. Improved knowledge of the main risk factors may, therefore, contribute to reduce the enormous risk burden in this population. Unlike most medical conditions, community surveillance has been the most common approach to evaluate the success of efforts to treat and control high BP, the most important factor susceptible of intervention. Although surveys are not a perfect evaluation tool, they are necessary to obtain information about BP control in the population.

**Perspectives**

Data provided in the present study reinforce the key role of BP control in reducing stroke mortality in the population and the necessity of further improving the BP control rates in the population >60 years of age. Blood pressure levels and rate of BP control appear as the overwhelming factors related to stroke mortality in the community, and whatever the burden of HT that has accumulated over a lifetime of exposure, the main determinant of stroke at the present is the effectiveness of antihypertensive treatment. The base rate of HT will also influence the risk among social groupings, but given the uniformly high rates of HT in different communities, such as those of the present study, measures to reduce BP will prevail in the first place as the cornerstone of stroke prevention. In addition, strategies to reduce HT-induced early organ damage, mainly LVH, should be considered.

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**Disclosures**

None.

**References**

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