Prevalence and Factors Associated With Circadian Blood Pressure Patterns in Hypertensive Patients
Alejandro de la Sierra, Josep Redon, José R. Banegas, Julián Segura, Gianfranco Parati, Manuel Gorostidi, Juan J. de la Cruz, Javier Sobrino, José L. Llisterri, Javier Alonso, Ernest Vinyoles, Vicente Pallarés, Antonio Sarría, Pedro Aranda and Luis M. Ruilope

Hypertension. 2009;53:466-472; originally published online January 26, 2009; doi: 10.1161/HYPERTENSIONAHA.108.124008

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/53/3/466

Data Supplement (unedited) at:
http://hyper.ahajournals.org/content/suppl/2009/01/26/HYPERTENSIONAHA.108.124008.DC1.html

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org/subscriptions/
Prevalence and Factors Associated With Circadian Blood Pressure Patterns in Hypertensive Patients

Alejandro de la Sierra, Josep Redon, José R. Banegas, Julián Segura, Gianfranco Parati, Manuel Gorostidi, Juan J. de la Cruz, Javier Sobrino, José L. Llistseri, Javier Alonso, Ernest Vinyoles, Vicente Pallarés, Antonio Sarría, Pedro Aranda, Luis M. Ruilope; on behalf of the Spanish Society of Hypertension Ambulatory Blood Pressure Monitoring Registry Investigators

Abstract—Ambulatory blood pressure (BP) monitoring has become useful in the diagnosis and management of hypertensive individuals. In addition to 24-hour values, the circadian variation of BP adds prognostic significance in predicting cardiovascular outcome. However, the magnitude of circadian BP patterns in large studies has hardly been noticed. Our aims were to determine the prevalence of circadian BP patterns and to assess clinical conditions associated with the nondipping status in groups of both treated and untreated hypertensive subjects, studied separately. Clinical data and 24-hour ambulatory BP monitoring were obtained from 42 947 hypertensive patients included in the Spanish Society of Hypertension Ambulatory Blood Pressure Monitoring Registry. They were 8384 previously untreated and 34 563 treated hypertensives. Twenty-four-hour ambulatory BP monitoring was performed with an oscillometric device (SpaceLabs 90207). A nondipping pattern was defined when nocturnal systolic BP dip was <10% of daytime systolic BP. The prevalence of nondipping was 41% in the untreated group and 53% in treated patients. In both groups, advanced age, obesity, diabetes mellitus, and overt cardiovascular or renal disease were associated with a blunted nocturnal BP decline (P<0.001). In treated patients, nondipping was associated with the use of a higher number of antihypertensive drugs but not with the time of the day at which antihypertensive drugs were administered. In conclusion, a blunted nocturnal BP dip (the nondipping pattern) is common in hypertensive patients. A clinical pattern of high cardiovascular risk is associated with nondipping, suggesting that the blunted nocturnal BP dip may be merely a marker of high cardiovascular risk. (Hypertension. 2009;53:466-472.)

Key Words: circadian blood pressure pattern • nocturnal blood pressure dip • cardiovascular risk factors • ambulatory blood pressure monitoring • hypertension

Clinic (office) blood pressure (BP) measurement has been the basis for the established relationship between elevated BP and cardiovascular morbidity and mortality.1–3 Clinic BP, however, may not necessarily represent an individual’s usual BP level. Ambulatory BP monitoring (ABPM) has become an efficacious instrument aiding therapeutic decisions in hypertensive patients and other subjects at risk of cardiovascular disease. Moreover, ABPM offers more accurate prognostic information of cardiovascular outcomes than office readings. This has been demonstrated clearly in population-based surveys4,5 and in both treated6–8 and untreated7,9,10 hypertensive subjects.

In addition to the mean 24-hour BP level, variation in the day-night BP pattern (the dipping status) has also been claimed as an important predictor of both target-organ damage and cardiovascular events.5,10–12 On average, each 5% attenuation in the decline in nocturnal systolic BP (SBP)/diastolic BP (DBP) conferred an ≈20% rise in the risk of cardiovascular mortality.11–13 Subjects with a blunted BP decrease (<10%) or even an increase in BP during the night were those to exhibit a worse cardiovascular prognosis.9,13–15

However, the magnitude of the proportion of different circadian BP patterns has not been noticed previously in large studies carried out in daily practice. This may have not only

Continuing medical education (CME) credit is available for this article. Go to http://cme.ahajournals.org to take the quiz.

Received October 1, 2008; first decision October 17, 2008; revision accepted December 24, 2008.

From the Hypertension Unit (A.d.l.S.), Hospital Clinic, University of Barcelona, Barcelona, Spain; Hypertension Unit, Hospital Clínico (J.R.), University of Valencia and Centro de Investigación Biomédica au Red (CIBER) of Obesity and Nutritional Disorders, Valencia, Spain; Department of Preventive Medicine and Public Health (J.R.B., J.J.d.l.C.), Autonomous University and CIBER of Epidemiology and Public Health, Madrid, Spain; Hypertension Unit (J.Segura, L.M.R.), Hospital 12 de Octubre, Madrid, Spain; Instituto Auxológico (G.P.), Hospital San Gennaro, Milan, Italy; Department of Nephrology (M.G.), Hospital San Agustín, Avilés, Spain; Department of Medicine (J.Sobrino), Hospital de L’Espirit Sant, Santa Coloma de Gramanet, Spain; Centro de Salud Ingeniero Benlloch (J.L.L.), Valencia, Spain; Centro de Salud Sillería (J.A.), Toledo, Spain; Centre d’Atenció Primària La Mina (E.V.), Barcelona, Spain; Unidad de Vigilancia de la Salud (V.P.), Unión de Mutuas, Castellón, Spain; Instituto de Salud Carlos III (A.S.), Madrid, Spain; and Hypertension Unit (P.A.), Hospital Carlos Haya, Málaga, Spain.

Correspondence to Alejandro de la Sierra, Hypertension Unit, Department of Internal Medicine, Hospital Clínica, Villarroel 170, E-08036 Barcelona, Spain. E-mail asier@clinic.ub.es

© 2009 American Heart Association, Inc.

Hypertension is available at http://hyper.ahajournals.org

DOI: 10.1161/HYPERTENSIONAHA.108.124008
clinical but also public health care relevance. Thus, the objectives of the present study were to determine the prevalence of circadian BP patterns and to assess clinical conditions associated with the nondipping status in groups of both treated and untreated hypertensive subjects, studied separately. For all of the above purposes, we used the Spanish Society of Hypertension ABPM Registry, which is an ongoing nationwide project based on a large-scale network of primary care physicians trained in ABPM.

Patients and Methods

Study Design

The Spanish Society of Hypertension ABPM Registry was developed to promote the use of ABPM in clinical practice. The ABPM Registry is based on the distribution of >900 ambulatory BP monitors, SpaceLabs 90207 (SpaceLabs Inc), for routine use by physicians from primary care centers and specialized units spread across the 17 autonomous communities covered by the public national health care system in Spain. Details of physician recruitment and characteristics of the registry have been reported previously. Briefly, physicians and nurses received specific training about the technique of ABPM and used the internet-based platform that receives ABPM registries together with their corresponding medical charts. Physicians then obtained a result report on real time, and registries were stored in a database from an external clinical research organization. The protocol was approved by a series of institutional review boards from the different autonomous communities of Spain, and patients gave informed consent. The registry is continuously growing, with the reception of data of ~1500 patients per month, with the first patient recruited in June 2004. For the purpose of the present study, 42 947 hypertensive patients (34 563 treated and 8384 untreated), recruited by 1126 physicians between June 2004 and December 2006, were selected.

Inclusion criteria were men and women aged ≥18 years of age with either an office BP ≥140 and/or 90 mm Hg obtained in ≥2 measurements without receiving any antihypertensive agent (untreated group; N=8384) or a documented diagnosis of essential hypertension, independent of office BP, under treatment with ≥1 antihypertensive drug stable for ≥2 months (treated group; N=34 563). Moreover, for the inclusion in the study, it was necessary to obtain valid ABPM information and reliable, complete data on all of the variables required for the intended analysis. The diagnosis of hypertension was obtained following the Spanish Society of Hypertension guidelines, which, for diagnosis and classification purposes, adopt the recommendations of the European Society of Hypertension/European Society of Cardiology. The practice guidelines of the European Society of Hypertension for BP measurement were used to establish indications for ABPM. Exclusion criteria were extreme obesity with an arm circumference >42 cm and atrial fibrillation or other cardiac arrhythmias, which may interfere with ambulatory BP measurements.

BP Measurements

BP was measured at the office with a calibrated mercury sphygmomanometer or a validated semiautomatic oscillographic device, after 5-minute rest in a sitting position. BP values were estimated as the mean of 2 readings. Thereafter, 24-hour ABPM was performed using the SpaceLabs 90207 automated noninvasive oscillometric device, programmed to register BP at 20-minute intervals for the 24-hour period. The majority of registries were performed on working days, programmed to register BP at 20-minute intervals for the 24-hour period. The majority of registries were performed on working days, and patients were instructed to maintain their usual activities, extended and immobile at the time of each cuff inflation. Valid registries were used to establish indications for ABPM.

Definition of Circadian Patterns

A normal dipping pattern (dipper) was diagnosed when the reduction in the average SBP during the night period was >10% of mean SBP during the day. When this proportion was >20%, the patient was classified as an extreme dipper. An abnormal dipping pattern (non-dipper) was diagnosed when the average SBP reduction was <10% with respect to day values. When the mean night SBP was higher than the day one, the patient was classified as a riser.

Study Variables

Variables collected for each patient based on the interviews and physical examination at the time of visit and on data drawn from clinical records were defined and measured in accordance with national and international guidelines. These included age, gender, weight, height, body mass index (BMI), duration of hypertension, known cardiovascular risk factors (eg, smoking habit, dyslipidemia, and diabetes mellitus), and clinical cardiovascular or renal disease (coronary heart disease, congestive heart failure, peripheral artery disease, cerebrovascular disease, or chronic renal failure). Details about antihypertensive treatment (generic name of drugs, and dosing time in a 3-category scheme: breakfast, lunch, and dinner) were collected in the group of treated patients.

Statistical Analysis

Data are presented as frequencies and percentages for qualitative variables and as means±SDs for quantitative variables. Differences in study variables between dipping and nondipping groups were assessed with the Pearson χ² for qualitative variables and the Student’s t test for quantitative data. The following variables were considered: age (<60 or ≥60 years); gender (male or female); time of day of clinical BP measurement (morning: 7:00 AM to 12:00 PM or evening: 12:00 PM on); duration of hypertension (in years); number of antihypertensive drugs used (1 or ≥2); time of day of antihypertensive drug administration (morning, evening, or morning and evening); obesity (BMI <30 or ≥30 kg/m²); tobacco smoking (yes or no); dyslipidemia (yes or no); diabetes mellitus (yes or no); and personal history of clinical cardiovascular disease or renal disease (yes or no). Associations are expressed as odds ratios with 95% CIs. Statistical significance was set at P<0.05. The relationships between Relative, nocturnal BP decline and study variables were assessed by multiple linear regression analysis. Variables significantly associated with nondipping status in the univariate analyses were subjected to multivariate analysis with a logistic regression procedure and forward stepwise selection if P value was <0.20 after univariate testing. The SPSS for Windows 13.0 software (SPSS Inc) was used for statistical analysis.

Results

General Characteristics of Patients Included

In the cohort of 8384 untreated patients, 55.6% were men, with a mean age of 53.2±13.8 years. Office SBP/DBP was 152.1±14.2/92.7±9.9 mm Hg, and 24-hour ambulatory BP was 132.0±12.7/80.8±9.6 mm Hg. Mean BMI was 28.1±4.4 kg/m². Cardiovascular risk factors included dyslipidemia in 27.5% of cases, diabetes mellitus in 9.3%, and current smoking in 21.1%. History of cardiovascular clinical conditions included coronary heart disease in 1.6%, stroke in 1.5%, congestive heart failure in 0.5%, and chronic renal disease in 0.3%.

In the cohort of 34 563 treated patients, 53% were men, and the mean age was 60.0±13.8 years. Office SBP/DBP was 149.5±19.3/87.8±11.7 mm Hg, and 24-hour ambulatory BP was...
Dipping status was not associated with the presence of isolated clinical hypertension ("white coat") in untreated patients or with isolated office resistance in the treated group, because the proportion of patients with 24-hour BP <130/80 mm Hg was similar in dippers and nondippers. In the cohort of patients receiving antihypertensive therapy, nondipping status was associated with the use of a greater number of drugs (P<0.001) but not with the time of the day when treatment was administered (P=0.352).

When the relative nocturnal BP decline was analyzed as a continuous variable, again, older patients, obese, nonsmokers, diabetics, and those with previous cardiovascular disease had a blunted SBP and DBP decline during the night (Tables S1 and S2, please see the online data supplement at http://hyper.ahajournals.org). Moreover, in the group of treated patients, BP decline was less pronounced in those treated with >1 agent but minimally influenced by the time of drug administration (Tables S1 and S2).

We performed a multiple linear regression analysis and found that blunted nocturnal SBP (Table 2) and DBP (Table S3) decline were associated with most of the variables that were statistically significant in the bivariate analysis, including age, gender, BMI, diabetes mellitus, and previous cardiovascular disease. Relationships were consistent in both treated and untreated patients, as well as in the entire cohort and for both SBP and DBP dip. The exceptions were female gender, which for diastolic dipping was only significant in the treated cohort, and nonsmoking, which was only significant for systolic dipping in treated patients.

Furthermore, the inclusion of the type of treatment (major classes of drugs, all possible combinations of 2 drugs and the combination of ≥3 drugs) did not significantly affect the variables associated with the nocturnal BP decline (data not shown). In the whole group and in those treated, a blunted nocturnal BP decline was also associated with a greater number of antihypertensive drugs (Table 2 and Table S3).

Finally, the results of the multiple logistic analysis also revealed a very close pattern of variables associated with the dipping status in both treated and untreated subjects, as well as in the entire cohort (Table 3). After adjusting for 24-hour SBP and DBP, age >60 years, and BMI >30 kg/m², diabetes mellitus and overt cardiovascular or renal disease were associated with the nondipping status. Moreover, in the group of treated patients, treatment with >1 antihypertensive agent was also associated with nondipping.

**Discussion**

The present study, carried out in a large population of both treated and untreated hypertensive outpatients attended in routine conditions of daily practice, showed that ~50% of hypertensives presented a blunted nocturnal BP decline. The proportion was lower in untreated patients (41%) and higher...
in the treated group (53%). Factors associated with a nondipping status, however, were consistently similar in both untreated and treated patients and related to an older age, other cardiovascular risk factors (eg, obesity and diabetes), and overt cardiovascular or renal disease. As a consequence of the blunted BP nocturnal fall, nocturnal BP values were significantly higher in nondipping hypertensives as compared with the dippers, even when no differences were present during the awake period.

In addition, some relevant information emerged from the group of patients receiving antihypertensive therapy. Despite the fact that antihypertensive treatment increased the probability of a nondipping pattern, whatever the time at which the medication is given, a blunted nocturnal BP decline was associated with the need for more antihypertensive drugs used for BP control.

There is no doubt regarding the importance of ABPM in the diagnosis and management of hypertension, as stated in international guidelines.\textsuperscript{12,21} Twenty-four-hour BP provides refined prognostic information regarding future cardiovascular outcomes in comparison with office or clinic BP\textsuperscript{14,16} and also helps in making therapeutic decisions in patients who exhibit discordance between clinic and ambulatory BP values (isolated office hypertension or resistance and masked hypertension).\textsuperscript{24} The Spanish Society of Hypertension ABPM Registry has contributed by extending the use of ABPM in primary practice. Furthermore, the large number of patients included in the registry has aided to collect relevant information about several ABPM-related parameters, as reflected in previous reports.\textsuperscript{16–20}

The relative prognostic importance of nocturnal BP decline has generated a great scientific interest.\textsuperscript{5,9,10–15,25} A blunted
nighttime BP decline is also regarded as a prognostic marker of cardiovascular events, both in hypertensive subjects\textsuperscript{7,9,11,15} and in the general population.\textsuperscript{12,13} Using a large cohort of patients from the ABPM Spanish database, we have observed that the amount of nocturnal BP decline was closely related to the level of risk. Nondipping was associated with advanced age, obesity, and diabetes mellitus, conditions that increase cardiovascular risk. Moreover, a history of previous cardiovascular or renal disease was more common in nondippers than in dippers.

It has been claimed that categorization of patients into dippers and nondippers is poorly reproducible\textsuperscript{26,27} and leads to some confusion when its relationship with potential clinical associated factors is examined. In the present study, however, the results obtained by categorization of patients into dippers and nondippers or by regarding the relative nocturnal BP decline as a continuous variable were essentially the same, thus enhancing the consistency of the observation.

Equally important is that clinical variables associated with a nondipping pattern were present in both treated and untreated patients. The multivariate analysis performed in the present study (the multiple linear regression using relative nocturnal BP decline as the dependent variable and the logistic regression of the variables associated with the dipping status) yielded similar results. In fact, most of the variables included in the analysis maintained their statistical significance, and the results were similar in treated and untreated patients, as well as in the entire cohort.

The proportion of nondipping status was higher and the relative nocturnal BP decline was blunted in the cohort of treated patients compared with the untreated one. This has been attributed to the use of antihypertensive treatment, which is commonly administered in the morning and lowers BP, especially during daytime.\textsuperscript{7,12} With the data of the present study, it seems to be an inaccurate assumption. When patients taking medication in the morning, in the evening, or twice a day were compared, no differences in the relative nocturnal BP decline were observed. Moreover, the proportion of patients receiving all or a part of their medication at night was not different between dippers and nondippers. Consequently,

Table 2. Results of Multiple Linear Regression Analysis of Independent Variables Associated With the Relative Nocturnal SBP Decline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Untreated Patients</th>
<th>Treated Patients</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Coefficient β (95% CI)</td>
<td>P</td>
<td>Coefficient β (95% CI)</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.089 (-0.098 to -0.079)</td>
<td>&lt;0.001</td>
<td>-0.130 (-0.148 to -0.130)</td>
</tr>
<tr>
<td>Female gender</td>
<td>-0.314 (-0.580 to -0.048)</td>
<td>0.021</td>
<td>-0.228 (-0.442 to -0.014)</td>
</tr>
<tr>
<td>BMI, kg/m(^2)</td>
<td>-0.093 (-0.123 to -0.063)</td>
<td>&lt;0.001</td>
<td>-0.092 (-0.114 to -0.069)</td>
</tr>
<tr>
<td>Smoking</td>
<td>NS</td>
<td>0.024</td>
<td>0.343 (0.045 to 0.641)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>-1.141 (-1.852 to -0.969)</td>
<td>&lt;0.001</td>
<td>-0.894 (-1.149 to -0.640)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>-2.076 (-3.043 to -1.109)</td>
<td>&lt;0.001</td>
<td>-2.183 (-2.565 to -1.801)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>-2.622 (-4.958 to -0.287)</td>
<td>0.028</td>
<td>-1.399 (-2.030 to -0.646)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>-1.465 (-3.345 to -0.176)</td>
<td>0.005</td>
<td>-1.487 (-1.954 to -1.019)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>NS</td>
<td>&lt;0.001</td>
<td>-1.339 (-2.032 to -0.646)</td>
</tr>
<tr>
<td>No. of antihypertensive drugs</td>
<td>NA</td>
<td>&lt;0.001</td>
<td>-0.683 (-0.785 to -0.581)</td>
</tr>
</tbody>
</table>

NS indicates not significant; NA, not applicable.

*Data are from 1 drug onward in treated patients and from 0 drugs onward in the entire group.

Table 3. Logistic Regression Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Untreated Patients</th>
<th>Treated Patients</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference</td>
<td>Odds Ratio (95% CI)</td>
<td>P</td>
<td>Odds Ratio (95% CI)</td>
</tr>
<tr>
<td>Age, ⩾60 y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;60 y</td>
<td>1.83 (1.66 to 2.02)</td>
<td>&lt;0.001</td>
<td>1.57 (1.47 to 1.67)</td>
</tr>
<tr>
<td>Female gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1.10 (1.01 to 1.19)</td>
<td>0.028</td>
<td></td>
</tr>
<tr>
<td>BMI, ⩾30 kg/m(^2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;30 kg/m(^2)</td>
<td>1.23 (1.12 to 1.35)</td>
<td>&lt;0.001</td>
<td>1.20 (1.13 to 1.26)</td>
</tr>
<tr>
<td>Current smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non smoker</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyslipidemia, present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus, present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>1.42 (1.24 to 1.62)</td>
<td>&lt;0.001</td>
<td>1.14 (1.06 to 1.22)</td>
</tr>
<tr>
<td>Overt cardiovascular or renal disease</td>
<td>1.63 (1.34 to 2.00)</td>
<td>&lt;0.001</td>
<td>1.52 (1.41 to 1.64)</td>
</tr>
</tbody>
</table>

Data show factors independently associated with nondipping status after adjustment by 24-hour SBP and DBP. NS indicates not significant; NA, not applicable.
the level of risk with higher proportions of elderly subjects, diabetics, and those with a history of cardiovascular or renal disease, in comparison with the untreated cohort, can explain the presence of nondipping. The need for more antihypertensive drugs in the nondipping group could also reflect the severity and the difficulty in treating elevated BP.

The present findings should be interpreted taking into account some limitations of the study, including the cross-sectional design, which precludes conclusions about causal relationships, and the classification of dippers and nondippers with a single 24-hour ABPM. The poor reproducibility over time of the classification of hypertensive patients into dippers and nondippers based on single ABPM has already been mentioned, but the concordance of the results obtained by looking at the night/day ratio as a continuous variable adds scientific validity to the results obtained. Furthermore, the large number of patients included in the analysis adds also strength to the observation of a high prevalence of a nondipping pattern and the identification of independent variables significantly associated with blunted BP decrease during the night.

Perspectives
The findings of the present study have implications in clinical practice. The circadian pattern was analyzed in the greatest cohort of patients with ABMP data obtained until now. In hypertensives, treated and nontreated, a worse cardiovascular risk profile, including advanced age, other risk factors, and diseases are the main factors associated with a blunted nocturnal BP decrease or a nondipping pattern. In this sense, this circadian pattern could be seen as a marker of high cardiovascular risk, helping to achieve more refined prognostic information. Although treated patients are more often nondippers, our results suggest that the level of risk could be the main responsibility of nondipping and not the treatment itself.

Acknowledgments
We thank all of those members of the Spanish Society of Hypertension Ambulatory Blood Pressure Monitoring Registry who participated in the study. The names of all of the participating practitioners have been published previously and are available at http://www.cardiorisc.com. We thank Marta Pulido, MD, for editing the article and for editorial assistance.

Source of Funding
The main funding for the study was obtained from Lacer Spain, SA, through an unrestricted educational grant.

Disclosures
None.

References


