

Hypertension

JOURNAL OF THE AMERICAN HEART ASSOCIATION



*Learn and Live*SM

Effectiveness of Blood Pressure Control Outside the Medical Setting

José R. Banegas, Julián Segura, Javier Sobrino, Fernando Rodríguez-Artalejo, Alejandro de la Sierra, Juan J. de la Cruz, Manuel Gorostidi, Antonio Sarría, Luis M. Ruilope and for the Spanish Society of Hypertension Ambulatory Blood Pressure Monitoring Registry Investigators

Hypertension 2007;49;62-68; originally published online Oct 30, 2006;

DOI: 10.1161/01.HYP.0000250557.63490.55

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75214

Copyright © 2007 American Heart Association. 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/cgi/content/full/49/1/62>

Subscriptions: Information about subscribing to Hypertension is online at
<http://hyper.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax: 410-528-8550. E-mail:
journalpermissions@lww.com

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

Hypertension Treatment and Control

Effectiveness of Blood Pressure Control Outside the Medical Setting

José R. Banegas, Julián Segura, Javier Sobrino, Fernando Rodríguez-Artalejo, Alejandro de la Sierra, Juan J. de la Cruz, Manuel Gorostidi, Antonio Sarría, Luis M. Ruilope; for the Spanish Society of Hypertension Ambulatory Blood Pressure Monitoring Registry Investigators

Abstract—We studied the effectiveness of blood pressure (BP) control outside the clinic by using ambulatory BP monitoring (ABPM) among a large number of hypertensive subjects treated in primary care centers across Spain. The sample consisted of 12 897 treated hypertensive subjects who had indications for ABPM. Office-based BP was calculated as the average of 2 readings. Twenty-four-hour ABPM was then performed using a SpaceLabs 90207 monitor under standardized conditions. A total of 3047 patients (23.6%) had their office BP controlled, and 6657 (51.6%) were controlled according to daytime ABPM. The proportion of office resistance or underestimation of patients' BP control by physicians in the office (office BP $\geq 140/90$ mm Hg and average daytime ambulatory BP $< 135/85$ mm Hg) was 33.4%, and the proportion of isolated office control or overestimation of control (office BP $< 140/90$ mm Hg and average daytime ambulatory BP $\geq 135/85$ mm Hg) was 5.4%. BP control was more frequently underestimated in patients who were older, female, obese, or with morning BP determination than in their counterparts. BP control was more frequently overestimated in those who were younger, male, nonobese, smokers, or with evening BP determination. Ambulatory-based hypertension control was far better than office-based hypertension control. This conveys an encouraging message to clinicians, namely that they are actually doing better than is evidenced by office-based data. However, the burden of underestimation and overestimation of BP control at the office is still remarkable. Physicians should be aware that the likelihood of misestimating BP control is higher in some hypertensive subjects. (*Hypertension*. 2007;49:62-68.)

Key Words: office blood pressure ■ ambulatory blood pressure ■ treatment goals ■ guidelines ■ control

Adequate control of hypertension is low in population and medical settings.¹⁻³ However, physicians frequently misclassify patients' blood pressure (BP) status at the office when compared with ambulatory BP monitoring (ABPM).⁴ In particular, BP readings are higher in standard clinical practice than in ambulatory readings.^{4,5} Nevertheless, the magnitude of the gap between office and ambulatory BP control has not been noted in large-scale studies addressing daily practice.

Furthermore, the prevalence and determinants of BP conditions, such as white-coat hypertension ([WCH] ie, high office BP with normal BP outside the medical setting) and masked hypertension (normal office BP with high BP outside the medical setting) have already been studied.⁶⁻¹⁴ However, WCH is a term reserved for those subjects not on antihypertensive treatment⁶; and in the case of treated hypertensive subjects, it would, therefore, be more accurate to use the term "office resistance,"⁶ that is, in-clinic

BP readings that are both higher than goal despite treatment and higher than normotensive BP outside the clinic as demonstrated by ABPM. Likewise, we focused on "isolated office control" (BP controlled at the office but uncontrolled on ABPM despite treatment) rather than masked hypertension. Office resistance and isolated office control are not usually reported but may well be common in daily clinical practice, because most hypertensive patients are, in fact, treated.

The effectiveness of BP control outside the office environment was examined for the first time by using ABPM in a large and varied sample of treated hypertensive subjects in primary care practice in Spain. We calculated the magnitude of the gap between office and ambulatory BP control. Furthermore, we also ascertained the burden of office resistance and isolated office control, that is to say, the magnitude of underestimation and overestimation of BP control, respectively, uncovered by ABPM. Finally, we

Received August 11, 2006; first decision August 28, 2006; revision accepted October 10, 2006.

From the Department of Preventive Medicine and Public Health (J.R.B., F.R.-A., J.J.d.I.C.), Autonomous University of Madrid, Madrid, Spain; the Hypertension Unit (J.S., L.M.R.), Doce de Octubre Hospital, Madrid, Spain; the Hypertension Unit (J.S.), Esperit Sant Hospital, Santa Coloma de Gramenet, Barcelona, Spain; the Hypertension Unit (A.d.I.S.), Clinic Hospital, Barcelona, Spain; the Nephrology Section (M.G.), San Agustín Hospital, Avilés, Asturias, Spain; and the Health Technology Assessment Agency (A.S.), Carlos III Institute of Public Health, Madrid, Spain.

Correspondence to José R. Banegas, Departamento de Medicina Preventiva y Salud Pública, Facultad de Medicina, Universidad Autónoma de Madrid, C/Arzobispo Morcillo 4, 28029 Madrid, Spain. E-mail joseramon.banegas@uam.es

© 2006 American Heart Association, Inc.

Hypertension is available at <http://www.hypertensionaha.org>

DOI: 10.1161/01.HYP.0000250557.63490.55

assessed clinical predictors of disagreement between office and ambulatory BP control. In particular, the influence exerted on these discrepancies by the time of day of office BP readings and drug administration has hardly been studied. All of this information is important for better knowledge of BP management in clinical practice and also for public health purposes. For all of the above purposes, we used the Spanish Society of Hypertension ABPM Registry, based on a large-scale network of Spanish physicians trained in ABPM.¹⁵ To our knowledge, this network of ≈ 900 clinical researchers using the same methodology to perform ABPM on $>36\,000$ outpatients is unique in the world.

Methods

Study Design and Patients

From June 2004 through April 2006, 1124 physicians from 210 primary healthcare clinics spread across the 17 geographic regions covered by Spain's national healthcare system were invited to participate. Physicians were chosen in proportion to the number of inhabitants in each geographic region; and within each region, selection of physicians also took into account their geographic dispersion in outpatient practice lists. Most of the physicians that were invited (897 [79.8%]) did in fact participate. The physicians consecutively recruited a total of 36 611 hypertensive patients (aged ≥ 18 years) who had conventional clinical indications for ABPM performance, resulting in a mean of 41 selected patients per physician. Physicians providing >1 ABPM per patient or <20 ABPMs were excluded from the study.

Of the patients recruited, 12 897 were evaluable patients with the following characteristics: (1) a documented diagnosis of essential hypertension, (2) attended at primary healthcare clinics, (3) treated with antihypertensive drugs, (4) followed-up by the same medical team for ≥ 2 months using the same study protocol, (5) <1 month elapsing between measurement of office BP and ABPM, and (6) valid BP and ABPM information and reliable, complete data on all of the variables required for the intended analyses.

Study Variables

In brief, BP was measured at the office with a calibrated mercury sphygmomanometer (in 70% of cases) or a validated semiautomatic device (30%), using appropriate cuffs (2 sizes), keeping the subject in a sitting position and ensuring standardized conditions.^{16,17} The average of 2 BP measurements was used for analyses. Thereafter, 24-hour ABPM was performed noninvasively on the nondominant arm, using a SpaceLabs model 90207 device and spacing the readings at 20-minute intervals.^{18,19} Patients were instructed to attend to their usual activities, return the following morning for device removal, and keep their arm extended and immobile at the time of each cuff inflation. For this study, ABPM was regarded as valid only if $\geq 80\%$ of systolic BPs (SBP) and diastolic BPs (DBP) during the daytime and nighttime periods (from subject diaries) were satisfactory. All of the valid recordings were analyzed to obtain average 24-hour, daytime, and nighttime SBP and DBP. The mean diurnal BP was used for analyses in this study. Physicians were trained and certified in ABPM.

Physicians also completed a questionnaire based on the interviews and physical examinations of patients at the time of visit and on data drawn from clinical records. The variables included, which were defined and measured in accordance with international guidelines, are listed in Table 1.^{16,17,20} We defined dyslipidemia as total serum cholesterol >250 mg/dL, low-density lipoprotein cholesterol >155 mg/dL, or high-density lipoprotein cholesterol <40 mg/dL in men and <48 mg/dL in women or the presence of current lipid-lowering therapy; obesity as body mass index ≥ 30 kg/m²; diabetes mellitus as fasting blood glucose repeatedly >126 mg/dL or current antidiabetic therapy; microalbuminuria as average urinary albumin excretion of

30 to 300 mg daily or albumin/creatinine ratio >22 mg/g in men and >31 mg/g in women and proteinuria as urinary protein excretion >300 mg daily; and left ventricular hypertrophy as left ventricular mass index calculated from an M-mode echocardiogram >125 g/m² in men or >110 g/m² in women or the presence of electrocardiographic criteria (Sokoloff index >35 mm). Renal disease was diagnosed when serum creatinine was >1.5 mg/dL in men and >1.4 mg/dL in women or when proteinuria was present. Biochemical parameters corresponded with the last office-based determination within the preceding 3 months.

The study was approved by institutional review boards at the coordinating reference centers, and written informed consent was obtained from all of the patients. The procedures followed were in accordance with institutional guidelines.

Statistical Analyses

Control of hypertension was evaluated by 2 methods, namely, the proportion of patients who reached BP goals with BP measured by conventional devices at the office (average office SBP/DBP: $<140/ <90$ mm Hg) and the proportion of patients who reached the BP goals as measured by ABPM (average daytime ambulatory SBP/DBP: $<135/ <85$ mm Hg).^{16–19} McNemar's χ^2 test was used to compare the proportion of BP control achieved with office versus ABPM methods. Concordance between both evaluation methods vis-à-vis BP control was assessed using the κ statistic. Taking ABPM-based control as the reference standard, patients were classified into the following groups: concordant BP control (BP control both at the office and on diurnal ABPM), concordant lack of control (control neither by office nor ABPM methods), false-negatives or office resistance (absence of control at the office but control by ABPM), and false-positives or isolated office control (control at the office but absence of control by ABPM). Clinical variables were compared with ANOVA or the χ^2 test, as appropriate. Statistical significance was set at $P < 0.05$.

Two separate logistic regression models were used to assess factors independently associated with the following 2 outcomes (dependent variables): office resistance or clinical underestimation of control (versus no underestimation) and isolated office control or clinical overestimation of control (versus no overestimation). Univariate analyses, using the Pearson χ^2 test, were used to assess whether each of the following (independent) variables was associated with the outcomes: age (≥ 60 years or <60), sex (female or male), time of day of clinical BP measurement (morning: 7:00 AM to 1:00 PM or evening: 1:00 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 night, or morning and evening or night), obesity (body mass index ≥ 30 kg/m² or <30 kg/m²), tobacco smoking (yes or no), dyslipidemia (yes or no), diabetes (yes or no), family history of premature cardiovascular disease (yes or no), target-organ damage ([TOD] atherosclerotic plaque, left ventricular hypertrophy, or microalbuminuria; yes or no), and associated clinical conditions (ischemic heart disease, stroke, heart failure, or chronic kidney disease; yes or no). Following the univariate analyses, clinical relevance and statistical significance criteria (univariate $P < 0.20$) were then used to select variables for multiple logistic regression. Variables with the highest P values were sequentially removed, and a new logistic model was defined without the eliminated variable. This operation was continued until all of the remaining variables had P values < 0.05 .

Two-sided tests were run, and statistical adjustment was made for multiple comparisons. Analyses were performed using the SPSS version 13 computer software program.

Results

The main sample characteristics are set out in Table 1. In brief, mean age was 61.9 ± 12.3 years (52.4% males), SBP/DBP at the office was $149.4 \pm 19.3/86.8 \pm 11.6$ mm Hg, and daytime ambulatory BP was $133.1 \pm 14.7/78.7 \pm 10.5$ mm Hg.

TABLE 1. Baseline Characteristics of Treated Hypertensive Patients According to BP Control

Variable	Total (N=12 897)	Concordant BP Control (n=2351)	Office Resistance (n=4306)	Isolated Office Control (n=696)	Concordant Lack of BP Control (n=5544)
Age, y	61.9 (12.3)	60.2 (12.4)	63.1 (12.0)	58.5 (12.7)	62.1 (12.2)
≥60 y, %	59.1	52.8	64.5	46.1	59.2
Male, %	52.4	50.3	45.8	58.6	57.5
Clinical SBP, mm Hg	149.4 (19.3)	126.3 (9.5)	152.4 (14.1)	129.4 (7.8)	159.5 (16.9)
Clinical DBP, mm Hg	86.8 (11.6)	77.0 (8.0)	87.7 (9.8)	78.7 (7.9)	91.3 (11.4)
BP taken in the morning, %	78.7	74.6	80.8	73.1	80.9
Daytime SBP, mm Hg	133.1 (14.7)	120.2 (8.3)	123.9 (7.7)	138.4 (9.6)	145.1 (11.5)
Daytime DBP, mm Hg	78.7 (10.5)	72.9 (7.4)	73.1 (7.5)	84.4 (8.8)	84.7 (10.2)
Duration of hypertension, y	7.8 (7.2)	6.7 (6.4)	8.0 (7.2)	7.0 (6.6)	8.3 (7.5)
No. antihypertensive drugs, %					
Monotherapy	39.1	42.4	36.8	44.0	38.9
2 drugs	35.0	34.9	36.1	32.3	34.5
≥3 drugs	25.9	22.7	27.1	23.7	26.6
Time of drug taking, %					
Morning only	80.2	79.4	81.8	80.9	79.2
Evening or night	9.9	10.6	9.2	9.4	10.3
Morning and evening or night	9.9	10.0	9.0	9.7	10.5
BMI ≥30 kg/m ² , %	40.3	38.3	44.1	30.3	39.5
Smokers, %	15.6	14.7	12.0	21.1	18.0
Dyslipidemia, %	42.2	43.6	42.1	42.2	41.7
Diabetes, %	21.5	18.3	20.6	20.3	23.8
Family history of premature CVD, %	11.9	12.4	11.0	11.6	12.4
Target-organ damage, %	17.3	15.1	15.0	18.0	19.4
History of CVD, %	15.3	18.2	14.9	16.2	14.3

Continuous values are shown as mean (SD). CVD indicates cardiovascular disease. See text for definitions of BP measurements. For definitions of clinical characteristics see Methods section.

For most patients (78.7%), office BP was determined in the morning. Approximately 39% of patients were on monotherapy, and 80% of patients took their pills in the morning only. The proportion of hypertensive subjects presenting with obesity, dyslipidemia, or ≥1 additional risk factor was >40%. Patients with office resistance were more frequently older, female, with morning BP determination, on multitherapy, and obese and were less likely to be smokers or have TOD ($P<0.05$). The opposite was true for patients with isolated office control.

Office Versus Ambulatory BP Control: Underestimation and Overestimation of BP Control

A total of 3047 patients (23.6%) had their office BP controlled, 6657 (51.6%) were controlled according to the ABPM method, and 2351 (18.2%) were controlled by both methods (Table 2). The proportion of office BP control was significantly different from that of ABPM control ($P<0.001$), and the κ index for intermethod agreement was 0.24. The proportion of false-negatives (office resistance) was 33.4% (95% CI: 32.6–34.2%), that is, physicians in the office underestimated patients' BP control in ≈33% of cases, and

the proportion of false-positives (isolated office control) was 5.4% (95% CI: 5.0–5.8%), meaning that physicians overestimated BP control in 5% of cases (Table 2 and Figure). Finally, 5544 patients (43.0%) were uncontrolled by both methods.

Population Estimates and Public Health Implications

An extrapolation to the national population of Spain was made to estimate the absolute number of hypertensive subjects in the 4 BP control groups at a Spanish population level, assuming universality of ABPM performance in the 8 million hypertensive subjects treated in outpatient clinics in Spain and that our sample was representative of that population.^{15,21} Approximately 1.9 million patients were clinically controlled (Figure). Of the 6.1 million persons with clinically uncontrolled hypertension, only 3.4 million were uncontrolled when ABPM was used, because the rest were false-negatives or "office resistant," and their BP control was, thus, underestimated at the office. Lastly, ≈1.5 of the 1.9 million clinically controlled patients were controlled by both methods, and ≈0.4 million were patients whose

TABLE 2. Control of BP Among Treated Hypertensive Subjects According to Office and Ambulatory BP Criteria

Office BP (SBP/DBP)	Daytime Ambulatory BP (SBP/DBP)		Total
	Controlled (<135/<85 mm Hg)	Uncontrolled (≥135/and/or ≥85 mm Hg)	
Controlled (<140/<90 mm Hg)	Concordant control 2351 18.2% (17.5–8.9%)	Isolated office control 696 5.4% (5.0–5.8%)	3047 23.6% (22.9–24.3%)
Uncontrolled (≥140/and/or ≥90 mm Hg)	Office resistance 4306 33.4% (32.6–34.2%)	Concordant lack of control 5544 43.0% (42.1–43.8%)	9850 76.4% (75.7–77.1%)
Total	6657 51.6% (50.7–52.5%)	6240 48.4% (47.5–49.3%)	12897 100%

Data correspond with number and percentage (95% CI) of patients.

BP control was overestimated using clinical measurements at the office.

Predictors of Disagreement Between Office BP and ABP Control

As can be seen in Table 3, multivariate analysis showed that BP control was more frequently underestimated in hypertensive patients who were older, female, obese, and with morning BP determination, or morning antihypertensive drug taking than in their counterparts and was less likely to be underestimated in those who were smokers or presented with diabetes or TOD. Likewise, multivariate analysis also showed that BP control was less likely to be overestimated in patients who were older, female, obese, or with morning BP taking or what amounts to the same thing; BP control was more frequently overestimated in subjects who were male, younger, nonobese, or with evening BP determination. Lastly, BP control in smokers was more likely to be overestimated.

Discussion

This is a study of the effectiveness of BP control outside medical settings using ABPM on a large number of treated hypertensive outpatients attended at multiple medical facilities spread across a developed country. This study

shows ABPM-based hypertension control as standing at ≈52%, a much better figure than that for office-based hypertension control (24%). In particular, the gap between office and ambulatory control was most marked among women (33%), older patients (32%), and those presenting with obesity (32%; data not shown). This conveys a reassuring message to practicing physicians, inasmuch as they are doing better in BP control than is believed on the basis of office- or population-based surveys, especially in Europe.^{2,3,22} Although the effectiveness of BP control does not exclusively depend on physicians, professional practices are at least as responsible as patient-related factors if not more so.³

The Burden of Undetected Controlled and Uncontrolled Hypertension: Clinical and Public Health Implications

Agreement between office- and ABPM-based methods of estimating BP control was poor (κ index=0.24). Physicians are, thus, prone to 2 types of bias when estimating BP control at the office, that is, false-negative (underestimation of BP control) and false-positive (overestimation).

In public health terms, the magnitude is higher for the underestimation bias. ABPM uncovers a large portion of hypertensive subjects (33.4%) whose BP control is not

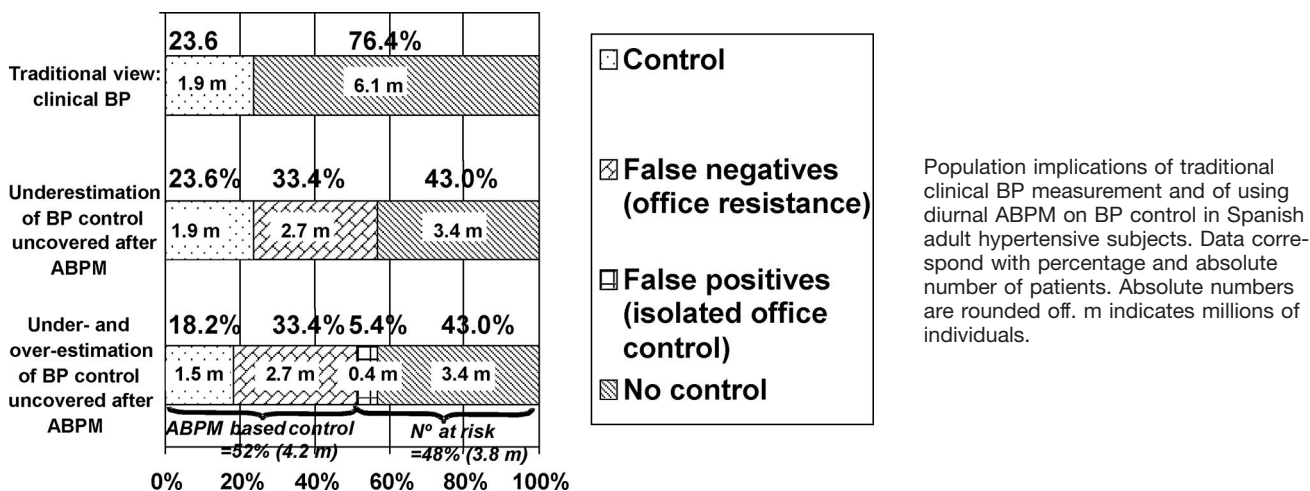


TABLE 3. Predictors of Underestimation and Overestimation of Control of Hypertension From Multivariate Logistic Analysis

Predictor	Odds Ratio (95% CI)	P
Underestimation		
Age (≥ 60 vs < 60 years)	1.33 (1.23–1.45)	< 0.001
Gender (female vs male)	1.37 (1.27–1.47)	< 0.001
BP determination (morning vs evening)	1.13 (1.03–1.24)	0.013
Drug taking (morning vs morning and evening or night)	1.14 (1.01–1.30)	0.038
Body mass index (≥ 30 kg/m ² vs < 30 kg/m ²)	1.25 (1.16–1.35)	< 0.001
Smoking (yes vs no)	0.78 (0.70–0.87)	< 0.001
Diabetes mellitus (yes vs no)	0.85 (0.78–0.93)	0.001
Target-organ damage (yes vs no)	0.90 (0.83–0.98)	0.014
Overestimation		
Age (≥ 60 vs < 60 years)	0.61 (0.52–0.71)	< 0.001
Gender (female vs male)	0.85 (0.72–0.99)	0.042
BP determination (morning vs evening)	0.73 (0.61–0.87)	< 0.001
Body mass index (≥ 30 kg/m ² vs < 30 kg/m ²)	0.64 (0.54–0.76)	< 0.001
Smoking (yes vs no)	1.23 (1.03–1.49)	0.026

Underestimation indicates absence of BP control by conventional method at the office but control by ABPM; overestimation, BP control by conventional method at the office, but absence of control by ABPM.

captured at the office. This office resistance represents the burden of “clinically undetected control.” Likewise, ABPM uncovers a relatively small portion of hypertensive subjects (5.4%) whose BP control is overestimated at the office. This isolated office control represents the burden of “clinically undetected lack of control.” Under extrapolation conditions, the sum of office resistance and isolated office control, or underestimation plus overestimation, totaling 3.1 million patients (or 39%) is the burden of misclassification of BP control. Finally, about half of treated hypertensive outpatients in Spain ($\approx 52\%$ or 4.2 million patients) are actually controlled, and the other half are in fact uncontrolled, thus forming the burden of hypertensive subjects at higher cardiovascular risk.

In clinical or individual terms, prognosis is worse for the overestimation bias, because it could lead to undertreatment of a substantial number of hypertensive subjects who, though apparently (clinically) controlled, are nonetheless at higher cardiovascular risk.^{23,24} In fact, individuals with isolated office control were more frequently on monotherapy than were other BP control groups. On the other hand, underestimation of BP control could lead to overtreatment. Individuals with office resistance were more frequently on multitherapy than were other BP control groups.

The prevalence of office resistance in treated hypertensive subjects was found to be similar to the prevalence of WCH reported in untreated individuals but often higher than that reported for treated or total patients in other studies.^{7–9} Nonetheless, there are large differences in the prevalence of this condition, and these studies are not

strictly comparable from a methodologic point of view. Interestingly, we observed a lower prevalence of isolated office control than the prevalence of masked hypertension reported in other studies.^{8,9,14} Although the selection of patients in our study may partially explain these differences, interstudy comparisons are inevitably difficult. Methodologic differences aside, in our study, as in the *Pressioni Arteriose Monitorate e Loro Associazioni* study in Italy, office resistance was much more common than isolated office control.¹⁰

Predictors of Disagreement Between Clinical BP Control and ABPM Control

Some factors partially explain the disparity between ABPM and office BP control in the present study. Some other studies have also reported that WCH is more frequent among older adults, females, nonsmokers, and obese patients.^{6,11,13} On the other hand, other studies have also reported factors selectively affecting ambulatory BP, including young age, male gender, and smoking.^{14,24}

Furthermore, measuring BP in the morning (versus the evening) was associated with a higher likelihood of office resistance and underestimation of BP control, as well as with a lower risk of overestimation of BP control. This suggests that antihypertensive drugs were not at their peak antihypertensive effect when BP was determined in the morning, and consideration should also be given to the fact that many drugs do not encompass a full 24-hour period.^{2,25,26} Likewise, taking antihypertensive drugs solely in the morning (versus taking them twice per day) was associated with a higher probability of office resistance and underestimation of BP control. This may be partially because of the fact that most BP determinations occurred in the morning.

Limitations

This study is not representative of the general Spanish hypertensive population but was rather intended to reflect the practice of physicians treating hypertensive subjects nationwide at primary care clinics situated throughout the Spanish healthcare system. Although further research is needed to confirm the generalizability of our findings, this study nevertheless selected a large, varied sample of physicians and patients with a wide range of characteristics and cardiovascular risk drawn from most regions of the entire country.

In this study, 2 BP readings from a single visit were averaged to characterize clinical BP, and the gap between ABPM-based and clinical BP control would probably be somewhat smaller if multiple visits had been used. However, we sought to reproduce the conditions of standard clinical practice surveys reporting hypertension control, where BP is usually determined at a single visit.^{2,3} Furthermore, some studies have reported that hypertension control was similar, regardless of whether a single BP measurement taken at 1 visit or the average of several measurements taken on different occasions was used.³ Although we used daytime ABPM means, 24-hour ambulatory BP yielded similar proportions of misclassification of BP control (data not shown).

The risk of being misclassified depends on the proximity to the cut point used to define clinic control. However, the

proportion of patients that were only misclassified on the basis of an office BP difference of <5 mm Hg (eg, an office SBP \geq 140 and <145 or DBP \geq 90 and <95 and ambulatory BP <135/<85) was only 8.4% (1085 hypertensive individuals), and even so, there would still be a marked gap between ambulatory BP control and clinical BP control (data not shown). To a certain extent, proximity to the cut point accounts for some of the factors that get selected as predictive of misclassification. However, for both the “SBP \geq 140 and <145 or DBP \geq 90 and <95” and the “SBP \geq 145 or DBP \geq 95 mm Hg” categories, most predictive factors remained statistically significant and with odds ratios in the expected direction (data not shown). However, the cross-sectional design of this study acts as a bar to inferring that the predictors identified are causal.

There is still some debate as to the appropriate level of daytime ABP equivalent to 140/90 mm Hg. For a lower ambulatory BP cutoff, for example, 130/80 mm Hg, 33.7% of patients had their BP controlled on ABPM. This figure is clearly lower than the 51.6% of patients with their ambulatory BP controlled when using the 135/85 mm Hg cut point, but it is still quite greater than the 23.6% of office BP control. Although we explicitly acknowledge that any difference in cutoff value will affect the resulting prevalence rates for misclassification, we have adopted the international consensus guidelines.

Perspectives

Control of hypertension using ABPM outside medical settings is much better than evidenced previously by office-based surveys. The traditional view based on clinical BP shows that only 24% of hypertensive subjects are controlled in our study, a figure quite similar to that found in other European and some US studies. Nevertheless, ABPM revealed that true BP control is more than double that figure. This conveys an encouraging message to clinicians, namely, that they are doing better than is usually thought.

However, ABPM likewise revealed that, at the office, BP control is underestimated by physicians in 1 of 3 hypertensive subjects and overestimated in 1 of 20 patients. In other words, the burden of undetected controlled and uncontrolled hypertension is still enormous. Hence, these data may also contribute to more efficient planning of health resources, because many hypertensive subjects believed previously to be uncontrolled are, in fact, controlled. However, the use of ABPM also leads to the emergence of undetected uncontrolled hypertensive subjects, putting them at high cardiovascular risk and implying additional costs. ABPM is rarely available at clinics, and an effort is, thus, needed to extend its use and indication in the future. Finally, a further implication of this study is that physicians should be aware both of their possibly inadequate assessment of BP control when this is purely based on office BP measurement and of the fact that the likelihood of misestimating BP control is higher in some hypertensive subjects.

Acknowledgments

We thank all those physicians (members of the Spanish Society of Hypertension ABPM Registry) who participated in this study. The

names of all participating practitioners have been published previously and are available at www.cardiorisc.com.

Source of Funding

The main funding for the study was obtained from Lacer Spain, SA, through an unrestricted educational grant. The funding body had no role in study design, analysis and interpretation of data, writing the report, or the decision to submit the article for publication.

Disclosures

None.

References

- Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005; 365:217–223.
- Llisterri JL, Rodríguez GC, Alonso FJ, Lou S, Divisón JA, Santos JA, Raber A, Castellar R, Ruilope LM, Banegas JR. Control de la presión arterial en la población hipertensa española atendida en atención primaria. Estudio PRESCAP 2002. *Med Clin (Barc)*. 2004;122:165–171.
- Wang TJ, Vasan RS. Epidemiology of uncontrolled hypertension in the United States. *Circulation*. 2005;112:1651–1662.
- Campbell NRC, Culleton BW, McKay W. Misclassification of blood pressure by usual measurement in ambulatory physician practices. *Am J Hypertens*. 2005;18:1522–1527.
- Little P, Barnett J, Barnsley L, Marjoram J, Fitzgerald-Barron A, Mant D. Comparison of agreement between different measures of blood pressure in primary care and daytime ambulatory blood pressure. *BMJ*. 2002;325: 254–259.
- Pickering TG. White coat hypertension. In: Izzo JL Jr, Black HR, eds. *Hypertension Primer: The Essentials of High Blood Pressure*. 3rd ed. Dallas, TX: American Heart Association; 2003:296–298.
- Martinez MA, García-Puig J, Martín JC, Guallar-Castillon P, Aguirre A, Torre A, Armada E, Nevado A, Madero RS. Frequency and determinants of white coat hypertension in mild to moderate hypertension: a primary care-based study. *Am J Hypertens*. 1999;12:251–259.
- Ungar A, Fumagalli S, Marini M, Di Serio C, Tarantini F, Boncinelli L, Baldereschi G, Valoti P, La Cava G, Olianti C, Masotti G, Marchionni N. Isolated ambulatory hypertension is common in outpatients referred to a hypertension centre. *J Hum Hypertens*. 2004;18:897–903.
- Ben-Dov IZ, Ben-Arie L, Mekler J, Bursztyjn M. In clinical practice, masked hypertension is as common as isolated clinic hypertension: predominance of younger men. *Am J Hypertens*. 2005;18:589–593.
- Bombelli M, Sega R, Facchetti R, Corrao G, Friz HP, Vertemati AM, Sanvito R, Banfi E, Carugo S, Primizia L, Mancia G. Prevalence and clinical significance of a greater ambulatory versus office blood pressure (“reversed white coat” condition) in a general population. *J Hypertens*. 2005;23:513–520.
- Dolan E, Stanton A, Atkins N, Den Hond E, Thijs L, McCormack P, Staessen J, O’Brien E. Determinants of white-coat hypertension. *Blood Press Monit*. 2004;9:307–309.
- Kotsis V, Stabouli S, Bouldin M, Low A, Toumanidis S, Zakopoulos N. Impact of obesity on 24-hour ambulatory blood pressure and hypertension. *Hypertension*. 2005;45:602–607.
- Verdecchia P, Palatini P, Schilacci G, Mormino P, Porcellati C, Pessina AC. Independent predictors of isolated clinic (“white coat”) hypertension. *J Hypertens*. 2001;19:1015–1020.
- Palatini P. Masked hypertension: how can the condition be detected? *Blood Press Monit*. 2004;9:297–299.
- Segura J, Sobrino J, Sierra C, Ruilope LM, Coca A. En representación de los investigadores del Proyecto CRONOPRES. Proyecto CRONOPRES: un nuevo enfoque para el control de la hipertensión arterial. *Hipertensión*. 2005;22:275–283.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jr, Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ, and the National High Blood Pressure Education Program Coordinating Committee. Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003;42:1206–1252.
- 2003 European Society of Hypertension-European Society of Cardiology. Guidelines for the management of arterial hypertension. *J Hypertens*. 2003;21:1011–1053.

18. Pickering TG, Hall JE, Appel LJ, Falkner BE, Graves J, Hill MN, Jones DW, Kurtz T, Sheps SG, Roccella EJ. Recommendations for blood pressure measurement in humans and experimental animals. Part 1: blood pressure measurement in humans. A Statement for Professionals From the Subcommittee of Professional and Public Education of the Am Heart Association Council on High Blood Pressure Research. *Hypertension*. 2005;45:142–161.
19. O'Brien E, Asmar R, Beilin L, Imai Y, Mancia G, Mengden T, Myers M, Padfield P, Palatini P, Parati G, Pickering T, Redon J, Staessen J, Stergiou G, and Verdecchia P on behalf of the European Society of Hypertension Working Group on Blood Pressure Monitoring. Practice guidelines of the European Society of Hypertension for clinic, ambulatory and self blood pressure measurement. *J Hypertens*. 2005;23:697–701.
20. World Health Organization. WHO MONICA Project. *MONICA Manual*. Geneva, Switzerland: World Health Organization; 1990.
21. Banegas JR. Epidemiología de la hipertensión arterial en España. *Hipertensión*. 2005;22:353–362.
22. Wolf-Maier K, Cooper RS, Kramer H, Banegas JR, Giampaoli S, Joffres MR, Poulter N, Primayesta P, Stegmayr B, Thamm M. Hypertension treatment and control in five European countries, Canada, and the United States. *Hypertension*. 2004;43:10–17.
23. Ohkubo T, Kikuya M, Metoki H, Asayama K, Obara T, Hashimoto J, Totsune K, Hoshi H, Satoh H, Imai Y. Prognosis of masked hypertension and white-coat hypertension detected by 24-h ambulatory blood pressure monitoring. 10-year follow-up from the Ohasama study. *J Am Coll Cardiol*. 2005;46:508–515.
24. Pierdomenico SD, Lapenna D, Bucci A, Di Tommaso R, Di Mascio R, Manente BM, Caldarella MP, Neri M, Cucurullo F, Mezzetti A. Cardiovascular outcome in treated hypertensive patients with responder, masked, false resistant, and true resistant hypertension. *Am J Hypertens*. 2005;18:1422–1428.
25. Redon J, Roca-Cusachs A, Mora-Macía J. Uncontrolled early morning blood pressure in medicated patients: the ACAMPA study. Analysis of the control of blood pressure using ambulatory blood pressure monitoring. *Blood Press Monit*. 2002;7:111–116.
26. Hermida RC, Calvo C, Ayala DE, Fernandez JR, Covelo M, Mojon A, Lopez JE. Treatment of non-dipper hypertension with bedtime administration of valsartan. *J Hypertens*. 2005;23:1913–1922.