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Preventing Misdiagnosis of Ambulatory Hypertension: Algorithm Using Office and Home Blood Pressures

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Abstract

Objectives—An algorithm for making a differential diagnosis between sustained and white coat hypertension (SH and WCH) has been proposed–patients with office hypertension undergo home blood pressure monitoring (HBPM) and those with normal HBP levels undergo ambulatory blood pressure monitoring (ABPM). We tested whether incorporating an upper office blood pressure (OBP) cutoff in the algorithm, higher than the traditional 140/90 mmHg, reduces the need for HBPM and ABPM.

Methods—229 normotensive and untreated mildly hypertensive participants (mean age 52.5 ± 14.6, 54% female) underwent OBP measurements, HBPM, and 24-hour ABPM. Using the algorithm, sensitivity (SN), specificity (SP), and positive and negative predictive values (PPV, NPV) for SH and WCH were assessed. We then modified the algorithm utilizing a systolic and diastolic OBP cutoff at a SP of 95% for ambulatory hypertension –those with office hypertension but OBP levels below the upper cutoff undergo HBPM and subsequent ABPM if appropriate.

Results—Using the original algorithm, SN and PPV for SH were 100% and 93.8%. Despite a SP of 44.4%, NPV was 100%. These values correspond to SP, NPV, SN, and PPV for WCH respectively. Using the modified algorithm, the diagnostic accuracy for SH and WCH did not change. However, far fewer participants needed HBPM (29 vs. 84) and ABPM (8 vs. 15).

Conclusions—In this sample, the original and modified algorithms are excellent at diagnosing SH and WCH. However, the latter requires far fewer subjects to undergo HBPM and ABPM. These findings have important implications for the cost-effective diagnosis of SH and WCH.

Keywords

Hypertension; office blood pressure; home blood pressure monitoring; ambulatory blood pressure monitoring

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Introduction

Elevated blood pressure is a strong, independent risk factor for incident cardiovascular disease [1]. Traditionally, the prognostic value of elevated blood pressure is based on the method of taking auscultatory measurements in an office setting [2]. However, compared to office blood pressures (OBP), ambulatory blood pressure (ABP) is a better predictor of target end-organ damage and cardiovascular events [3,4,5]. Further, not all patients who receive a diagnosis of hypertension on the basis of OBP assessments actually have elevated ABP levels, measured by ABP monitoring (ABPM) [6]. These issues pose a difficult diagnostic dilemma for clinicians who are seeking to differentiate patients with sustained hypertension (SH, office and ambulatory hypertension) from those with "white coat" hypertension (WCH, office hypertension with normal ABP levels), for whom antihypertensive drug treatment may be inappropriate.

Because of the obvious advantages of ABPM, it is considered by most researchers and clinicians to be the "gold standard" methodology for the non-invasive assessment of blood pressure, and is recommended for the differential diagnosis of SH and WCH [6,7]. However, ABPM is too expensive and impractical to be used for all patients presenting with office hypertension. It has been suggested that home blood pressure monitoring (HBPM) is a viable alternative [2,8]. As with ABP, the risks of target end-organ damage and cardiovascular events are more strongly associated with home blood pressure (HBP) than with OBP [9,10,11]. Additionally, HBPM is affordable, practical, and widely available. Thus, HBPM may be a useful alternative to ABPM for the assessment of SH and WCH.

In 1990, Dr. Thomas Pickering proposed an algorithm in which HBPM is used as a screening test in patients who are diagnosed with office hypertension - those with elevated HBP would be assumed to have SH, and those with normal HBP would undergo ABPM for a definitive diagnosis [12]. Such an algorithm, if implemented, could have important implications for the assessment of SH and WCH. However, a recent study by Stergiou et al. [13] suggested that this strategy has limited diagnostic value for identifying WCH. Therefore, other than performing ABPM in all patients with office hypertension, the most efficient and accurate way to diagnose SH and WCH remains unknown.

Some evidence suggests that there is an upper level of OBP, higher than the traditional 140/90 mmHg, that makes ambulatory hypertension more likely [14,15,16,17,18]. While there are obvious pitfalls in relying on OBP alone, the identification of an upper OBP threshold might obviate the need for performing HBPM as well as subsequent ABPM in patients whose OBP was above the threshold. However, the predictive value of an upper cutoff for OBP for identifying ambulatory hypertension remains poorly characterized. Further, whether an OBP cutoff would improve the efficiency and accuracy of the diagnostic algorithm remains unknown. Therefore, the aim of the present study was to assess the predictive value of a higher OBP cutoff in the diagnosis of ambulatory hypertension, and to determine the value of incorporating an upper OBP cutoff in the proposed algorithm to differentiate SH from WCH.

Methods

Subject Recruitment

This study was conducted as previously described [8,19]; the relevant methods are briefly described here. Participants were eligible if they: (1) were normotensive or had Stage 1 hypertension (140–159 mmHg/90–99 mmHg), according to Joint National Committee (JNC VI) criteria, (2) were aged 18 to 80 years, (3) were willing, with physician's permission, to come off antihypertensive medication (if treated) for 2 weeks prior to the first study visit, and to remain off for the duration of the study, and (4) had no history of overt cardiovascular disease.

Hypertensive participants were recruited from the Weill Cornell Hypertension Center of New York Presbyterian Hospital and from the Hypertension Center at Mount Sinai Medical Center in New York City. Normotensive participants were recruited through advertisements. Written informed consent was obtained from all subjects, and the study was approved by the Institutional Review Boards of Weill Medical College of Cornell University and Mount Sinai School of Medicine.

A total of 329 participants, enrolled between June 1998 and August 2003, underwent measurements of OBP and ABPM. HBPM was performed in a subset of 229 subjects. Table 1 shows the baseline characteristics of the study population (n=229), including their average systolic and diastolic blood pressures (SBP, DBP) measured at the office, by ABPM, and by HBPM.

Study Procedures

The study consisted of three visits, separated by one-month intervals. Each study visit occurred over two consecutive days (Days 1 and 2). On the first study visit, starting on Day 1, ABP measurements were performed using an oscillometric ABP monitor (SpaceLabs Model 90207, Redmond, WA) over a period of 36 hours. For about three-quarters of the recordings, the ABPM was programmed to take a blood pressure reading every 30 minutes throughout the monitoring period. For the remaining recordings, measurements were taken at 15-minute intervals, between 6 A.M. and 10 P.M, and every 30 minutes between 10 P.M. and 6 A.M. For the present analyses, we restricted the ABPM readings to the first 24 hours. Awake SBP and DBP levels were defined based on diary reports of the times subjects woke up and went to sleep. The mean number of valid measurements used to compute the mean awake ABP measures was 33.4±11.8.

The subject, still wearing the ABP monitor, returned the next day (Day 2) to the Hypertension Clinic where physician-obtained OBP readings were taken. The participant was escorted into an examination room and rested for at least 5 minutes in the seated position, after which the physician entered and took three OBP measurements using a mercury column sphygmomanometer and stethoscope. The same physician (TGP) took the mercury-column BP measurements on all occasions. For all OBP measurements, the participant sat in a straight-backed chair with adjustable armrests. The participant sat with feet uncrossed on the floor, and the arm supported at heart level, using the adjustable arm supports. The participant then left the Hypertension Clinic, still wearing the ABPM, which s/he was instructed to remove at bedtime that evening, and return via a prepaid mailer.

After the initial ABP recording, HBPM was performed over a 10-week period using, an automatic, oscillometric HBP monitor (Omron HEM-747 IC, Omron Health Care, Vernon Hills, IL), which has previously been validated [20,21,22]. The HBP monitor contained a built-in modem that provided a telephone link to a server located at LifeLink Monitoring, Inc. (Bearsville, NY) [23,24]. The monitor time- and date-stamped each reading, and could store up to 125 readings in memory. Readings could not be edited by the participant. Once the measurements were received by the server, a report was generated and faxed to our laboratory. Participants were instructed to take three HBP measurements on four days a week in the morning and again in the evening; they were also asked to take three additional measurements on two occasions (at mid-morning and mid-afternoon) on two days a week, for a total of 36 measurements a week. The mean number of valid HBP readings per subject was 267.2±115.4. For our study, analyses were performed with the HBP levels averaged over the first 12 assessments. A recently published systematic review [25] and an AHA/ASH/PCNA scientific statement [26] concluded that the minimum number of home measurements, needed to obtain a reliable estimate of a subject's usual blood pressure, is 12. Results for these analyses were not different than with the full set or an intermediate number (i.e. 30) of HBP readings.

ABP and OBP assessments were repeated at the second and third study visits. For the purposes of this study, the following blood pressures were utilized in the analyses: OBP measurements performed at the first and second visits (for a total of 6 readings), ABP measurement performed at the first study visit, and the HBP measurements. Office hypertension was defined as a persistently elevated OBP (SBP ≥140 mmHg or DBP ≥90 mmHg), accordingly to the mean of the 3 blood pressures at each study visit. Awake ambulatory hypertension and home hypertension were defined as SBP ≥135 or DBP ≥85 mmHg, based on internationally accepted limits [2,27]. SH was defined as meeting criteria for both office hypertension and ambulatory hypertension. WCH was defined as meeting criteria for office hypertension but having normal awake ABP levels.

Statistical Analyses

Results are presented as mean ± SD. Fisher's exact test and independent samples t-tests were used to compare proportions and means respectively. We used receiver-operating-characteristic (ROC) curves [28] to identify systolic and diastolic OBP cutoffs (using the mean of the 6 blood pressures from both study visits) for the diagnosis of ambulatory hypertension. Because combinations of systolic and diastolic OBP are likely to have independent predictive values, we incorporated both blood pressure measures in the ROC curve analysis, instead of using either systolic or diastolic OBP. Logistic regression was used to predict awake ambulatory hypertension from systolic and diastolic OBP. Predicted probabilities for ambulatory hypertension were then generated for each subject based on his/her systolic and diastolic OBP levels. A ROC curve analysis was used to determine sensitivities and specificities for different predicted probability cutoffs for ambulatory hypertension. We determined the probability cutoffs that yielded a specificity of 95% or greater for ambulatory hypertension (or equivalently a sensitivity of 95% or greater for normal ABP). A specificity of 95% for ambulatory hypertension is equivalent to a false positive rate of 5%. The SBP and DBP boundary, representing the probability cutoff that yielded a specificity of 95% for ambulatory hypertension, was then estimated by using the logistic regression equation: $\ln(\text{cutoff } p/(1-\text{cutoff } p)) = \beta_{sysOBP}(\text{systolic OBP}) + \beta_{diasOBP}(\text{diastolic OBP}) + \text{intercept}$. Using this equation, one can generate the upper boundary in a graph by calculating systolic OBP values (on the ordinate axis) from diastolic OBP values (on the abscissa axis), because the probability cutoff, β_{sysOBP}, $\beta_{diasOBP}$, and the intercept are known.

In participants with office hypertension (persistently elevated systolic OBP ≥140 or diastolic OBP ≥90 mmHg), the proposed strategy of first using HBPM as an initial screening test and then performing ABPM only in those with normal HBP levels (SBP <135 and DBP <85 mmHg), was assessed [12]. The algorithm was then re-examined by utilizing HBPM as a screening test only in those participants with office hypertension whose mean OBP levels were below the 95% specificity boundary for ambulatory hypertension.

Results

The sample was middle aged, and 54.1% were female (see Table 1). There were not significant differences between OBP (average of the six OBP measurements) and HBP levels for SBP [0.3 (95% CI −1.6 to 2.3) mmHg, p=0.75] or DBP [0.8 (95% CI −0.6 to 2.1) mmHg, p=0.28]. Systolic HBP levels were 1.6 (95% CI 0.1 to 3.1) mmHg lower than awake ABP (p=0.04). For DBP, there was not a significant difference between HBP and awake ABP levels [−0.7 (95% CI −1.9 to 0.4) mmHg, p=0.21]. Additionally, no significant differences were observed between OBP and awake ABP levels for SBP [−1.3 (95% CI −3.1 to 0.6) mmHg, p=0.18] or DBP [−0.0 (95% CI −1.1 to 1.1) mmHg, p=0.99].

In the 84 participants with office hypertension, mean OBP levels (average of the six OBP measurements) were 154 ± 14/92 ± 9 mmHg. HBP levels were 8.5 (95% CI 4.9 to 12.1) mmHg

and 5.3 (95% CI 2.8 to 7.9) mmHg lower than OBP levels for both SBP and DBP respectively (ps<0.001). There were no differences between HBP and awake ABP levels for SBP [−0.1 (95% CI −3.0 to 2.9) mmHg; p=0.96] or DBP [−0.5 (95% CI −2.9 to 1.9) mmHg; p=0.65]. Finally, OBP levels were 8.4 (95% CI 5.1 to 11.8) mmHg and 4.8 (95% CI 2.9 to 6.7) mmHg higher than awake ABP levels for both SBP and DBP respectively (ps<0.001).

95% Specificity Cutoff in OBP Levels for Identifying Participants with Ambulatory Hypertension

As expected, both systolic and diastolic OBP were significant independent predictors of ambulatory hypertension [OR 1.40 (95% CI 1.22–1.60) for each 5 mmHg increase in SBP, p<. 001; OR 1.38 (95% CI 1.10–1.72) for each 5 mmHg increase in DBP, p=.004]. Figure 1 shows the ROC curve summarizing the ability of different combinations of systolic and diastolic OBP levels to correctly diagnose ambulatory hypertension. The area under the ROC curve (equivalent to the C-index) is 0.863. Figure 2 shows the scatterplot of systolic OBP versus diastolic OBP. The 95% specificity boundary for ambulatory hypertension is shown in the scatter plot (solid line, Figure 2). By design, only 5% of the participants with ambulatory normotension (solid circles, Figure 2) had OBP levels above this line (Region A). Of the 229 participants (Regions A and B, Figure 2), 57 (24.9%) had systolic and diastolic OBP in Region A. For these 57 participants, the mean systolic and diastolic OBP were 159 ± 12 mmHg and 96 ± 7 mmHg respectively. Systolic and diastolic OBP ranged from 141 to 204 mmHg, and 83 to 112 mmHg, respectively. In addition, 55 (96.5%) of the 57 participants in Region A had office hypertension; and 52 (91.2%) had ambulatory hypertension (crosses, Figure 2) - this percentage represents the positive predictive value of using the 95% specificity OBP cutoff for the diagnosis of ambulatory hypertension.

Identifying Participants with Sustained Hypertension and White Coat Hypertension Using the Original Algorithm

Figure 3 shows the breakdown of participants depending on diagnosis by OBP assessment, HBPM, and ABPM. Of the 84 subjects with office hypertension, 75 (89.3%) had SH and 9 (10.7%) had WCH. Based on our original algorithm, which proposes HBPM for everyone with elevated OBP levels, and ABPM only if HBP levels are normal, 15 subjects would have ABPM and 11 of these (73%) would be found to have ambulatory hypertension, and hence SH. The sensitivity and positive predictive value of this algorithm for detecting SH are 100% (75/75; 95% CI 96–100%) and 93.8% (75/80; 95% CI 88–98%) respectively. Although the specificity for diagnosing SH is only 44.4% (4/9; 95% CI 15–77%), the negative predictive value is 100% (4/4; 95% CI 40–100%). Conceptually, the sensitivity, specificity, positive predictive value, and negative predictive value for the diagnosis of SH are equivalent to the specificity, sensitivity, negative predictive value, and positive predictive value respectively for the diagnosis of WCH. Hence, the sensitivity and positive predictive value for WCH are 44.4% and 100% respectively. Also, the specificity for diagnosing WCH is 100% and the negative predictive value is 93.8%.

Identifying Participants with Sustained Hypertension and White Coat Hypertension Using the 95% Specificity Boundary in OBP Levels for Ambulatory Hypertension

Figure 4 shows the breakdown of participants after modifying the algorithm utilizing the 95% specificity boundary for ambulatory hypertension. Of the 84 participants with office hypertension, 55 (65.5%) had OBP levels above this boundary - 51 (92.7%) of the 55 subjects had SH. Given that the modified algorithm does not mandate HBPM nor ABPM for these latter subjects, out-of-office testing would be performed in many fewer people, compared to the original algorithm (Figure 3 and 4; 29 vs. 84 for HBPM and 8 vs. 15 for ABPM). Further, the sensitivity and positive predictive value of the modified algorithm for SH are similar to the

original algorithm: 100% (75/75; 95% CI 96–100%) and 92.6% (75/81; 95% CI 84–97%) respectively. Although the specificity for diagnosing SH is only 33.3% (3/9; 95% CI 9–69%), the negative predictive value is 100% (3/3; 95% CI 31–100%). Equivalently, the sensitivity and positive predictive value for WCH are 33.3% and 100% respectively. Also, the specificity for diagnosing WCH is 100% and the negative predictive value is 92.6%.

Discussion

Our study confirms that ambulatory hypertension is more common in patients with higher levels of OBP [14,15,17,18]. We have also used an ROC curve analysis to demonstrate that we can utilize both systolic and diastolic OBP levels to identify a 95% specificity cutpoint that minimizes the false positive rate (5%) and maximizes the positive predictive value (91.2%) for the diagnosis of ambulatory hypertension, making SH likely and WCH unlikely.

In those diagnosed as hypertensive based on OBP levels, the original diagnostic algorithm has excellent sensitivity, and positive and negative predictive values for SH; and, equivalently, excellent specificity, and positive and negative predictive values for WCH. Having identified a cutpoint for OBP which makes ambulatory hypertension very likely, the results of our study suggest that it would be advantageous to incorporate this OBP cutpoint into the proposed algorithm to diagnose SH and exclude WCH. By doing so, it may be possible to avoid out-of-office testing with either HBPM or ABPM, for diagnostic purposes, in a large proportion of patients with office hypertension. Further, the predictive values for both SH and WCH remain excellent, suggesting an advantageous cost-effectiveness ratio for the newly proposed algorithm.

HBPM has been proposed as an adjunct to OBP measurements in the clinical setting [29,30]. The rationale behind this approach is the difficulty of conducting ABPM in all patients with office hypertension. Also, the ease and lower cost of HBPM makes it an ideal diagnostic test prior to ABPM. Further, many HBP monitors have passed the British Hypertension Society and American Association of Medical Instrumentation validation criteria [31,32]. In our study, approximately 70–80% of the participants who undergo HBPM (Figures 3 and 4) may be able to avoid ABPM because of the presence of home hypertension, a large proportion of whom also have SH. Similar diagnostic accuracy of HBPM in predicting ambulatory hypertension or normotension in those with office hypertension has been observed in other studies [33,34, 35]. In our study, a small percentage of the participants diagnosed with home hypertension have normal ABP levels (Figures 3 and 4). However, these participants, technically labeled as having WCH (office hypertension with normal ABP levels), may still be at increased risk for cardiovascular events, as recent evidence suggests that elevated HBP levels are associated with increased cardiovascular mortality, independent of ABP [36]. Therefore, HBPM may be both a valuable diagnostic and prognostic test for patients presenting with office hypertension.

One potential limitation of the original and modified algorithms is that the specificity for SH, and sensitivity for WCH are low. However, the positive and negative predictive values for both SH and WCH are high. The excellent positive predictive value for SH is explained by both a high true positive rate and a relatively low prevalence of WCH in our sample (10.7% of the participants with office hypertension). The high negative predictive value is explained by a very low false negative rate. Similarly, for the diagnosis of WCH, the sensitivity is low, yet the positive predictive value is high - this is explained by a low false positive rate. The high negative predictive value is additionally explained by a high true negative rate and relatively low prevalence of WCH in this sample.

Although the prevalence of WCH in our sample is consistent with a number of published studies [37,38,39], other studies have reported a higher prevalence of WCH [40,41,42]. In a previous

study by Stergiou et al. [13] that tested the original algorithm in untreated patients with office hypertension, similar specificity (100%), sensitivity (61%), and positive predictive value (100%) for WCH were observed. However, in contrast, the negative predictive value of the algorithm for WCH was lower (77%) than observed in our study (94.9%). The modest negative predictive value in the study by Stergiou et al. [13] is most likely explained by a much higher prevalence (38%) of WCH in their sample. Assuming a 38% prevalence of WCH in our study, but the same sensitivity (44.4%) and specificity (100%), we find that the negative predictive value falls from 93.8% to 78%, which is consistent with the findings by Stergiou et al [13]. Therefore, in a population in which the prevalence of WCH is higher, it is easier to diagnose, but at the same time, more difficult to exclude. Conversely, SH is easier to exclude, but also is more difficult to diagnose. Thus, the utility of the algorithm must be put in context of the underlying prevalence of WCH in the population being evaluated.

There are a number of explanations as to why the prevalence of WCH was relatively low in our study. OBP measurements can be substantially affected by differences in subject preparation, arm position, cuff placement, number of readings, number of visits, and the number and type (trained vs. untrained) of observers [2,26,43]. In our study, OBP readings were obtained by the same trained physician with the careful preparation of the subject and use of standardized measurement techniques. Also, three OBP readings were obtained at each of two visits. Data suggest that repeated OBP assessments reduce the prevalence of WCH [44]. This latter factor probably played an important role in our study. Office hypertension was defined as a persistently elevated systolic OBP ≥140 mmHg or diastolic OBP ≥90 mmHg, based on the mean of the 3 blood pressure readings at each visit. When we redefine office hypertension as an elevated OBP (≥ 140/90 mmHg) at the first visit only, we find that instead of 84 participants, 110 participants are diagnosed as having office hypertensive, and 19 (17.3%) of these participants have WCH. While this relaxed criterion for office hypertension increases the likelihood of having WCH, our original approach is more consistent with published guidelines, which recommend the performance of high quality OBP measurements, over multiple visits, in order to diagnose office hypertension [2,26,43].

It is noteworthy that the study by Stergiou et al. [13] was also conducted under carefully controlled conditions, yet a WCH prevalence of 38% was noted. However, the study was based on data from an earlier study conducted by Stergiou et al. [45] in which a prevalence rate of 11% for WCH (our prevalence was 10.7%) was observed when using similar OBP and ABP cutoffs as in our study. The reasons for the difference in WCH prevalence rates are unknown but may be explained by how office hypertension and ambulatory hypertension were defined, which differed somewhat across the 2 studies [13,45].

Overall, for the assessment of SH and WCH, the original and modified versions of the algorithm may have the greatest utility in populations where lower rates of WCH may be seen [15,37, 38,39]. Based on our results, it is tempting to recommend using Figure 2 and the modified algorithm in routine clinical practice for diagnosing SH (and excluding WCH) in patients presenting with elevated OBP levels. However, our analysis should be replicated in larger outpatient clinic samples prior to the widespread dissemination of this diagnostic strategy. Readings obtained from OBP assessments may be more variable in clinical practice than within the context of a research study. However, we believe that this variability is minimized when standard recommendations about OBP measurements are followed, as strongly suggested by our study. Thus, the performance of multiple, high quality measurements of OBP is not simply an adjunct, but is an essential part of a sound diagnostic algorithm for SH and WCH.

Finally, no differences in OBP and awake ABP levels were seen in the entire sample. This finding may seem unusual since other studies have shown that physician-measured blood pressures (OBP) are higher than awake ABP levels (i.e. a positive white coat effect). However,

a positive white coat effect is generally observed in hypertensive individuals [16,46,47], whereas either no or a negative white coat effect tends to be observed in normotensive individuals [16,48]. It is important to note that our sample included subjects with normal OBP, and in the 84 subjects with office hypertension, we indeed find a positive white coat effect. This is consistent with the study by Verdecchia et al. [16] demonstrating that the positive white coat effect is disproportionally seen in patients with office hypertension, and that the magnitude of the white coat effect increases with higher levels of OBP. Nevertheless, the prevalence of white coat hypertension in patients with office hypertension decreases with increasing levels of OBP, despite a greater white coat effect, due to a concomitant higher prevalence of ambulatory hypertension. Results from an international database also showed that higher levels of OBP are associated with higher ABP levels in hypertensive subjects [17,18]. Our results are completely consistent with these findings.

A few potential limitations of our study should be noted. First, we have considered one ABP assessment as the ”gold standard” for the diagnosis of ambulatory hypertension. Although some variability between monitoring sessions inevitably occurs, we chose to limit the ABP assessment to one 24-hour period as a number of studies have found high test-retest reliability for ABP levels [49,50]. Further, this approach is consistent with most of the studies linking ABP levels to cardiovascular outcomes [3,5,51], and also with the way ABPM is most commonly used in clinical practice. Second, in our study, the same diagnostic threshold (i.e. 135/85 mmHg) was used to classify home and ambulatory hypertension respectively. However, it is generally accepted that the diagnostic threshold for both HBP and awake ABP is 135/85 mmHg [52,53]. Third, in our study, HBPM was originally based on hundreds of readings over a 10-week period, however, we chose to limit the analyses to the first 12 HBP readings for a number of reasons. The performance of hundreds of readings may not be feasible for many patients. Further, a recently published systematic review [25] and scientific statement [26] both concluded that the minimum number of home measurements required for a reliable estimate of a subject’s average blood pressure is 12. Additionally, analyses were performed with the full set of HBP readings as well as the HBP levels averaged over 30 assessments, and the results were similar (data not shown). Fourth, our ROC curve analysis was conducted in all 229 participants rather than in the 84 participants with office hypertension; we did this in order to obtain the most robust possible estimates of the relationship of OBP to ambulatory hypertension. Excluding those with normal OBP, some of whom have ambulatory hypertension could have biased the results. Nevertheless, an additional ROC analysis, restricted to those with office hypertension was performed. While the diagnostic accuracy of the algorithm was similar (data not shown), an additional 17 participants were required to undergo out-of-office testing (HBPM and ABPM).

In conclusion, our findings suggest that the algorithm originally proposed in 1990 [12] is a valid strategy for the assessment of SH and WCH in patients presenting with office hypertension. The likelihood of ambulatory hypertension and SH increases at higher levels of OBP. Further, we have demonstrated that incorporation of a higher OBP cutoff in the diagnostic algorithm maintains the positive and negative predictive values while substantially decreasing the number of patients that require out-of-office testing with HBPM and ABPM. In our sample, the implementation of this modified algorithm would result in 65% fewer HBPM and 47% fewer ABPM recordings needing to be performed, making it substantially a more cost-effective strategy. We acknowledge that the negative predictive value for excluding WCH will be lower in populations where the prevalence of WCH is high - a phenomenon that is characteristic of all diagnostic tests [54,55]. Of course, both diagnostic algorithms require that OBP readings be obtained by careful and standardized measurement techniques. Future research is needed to validate our proposed upper OBP cutoffs, greater than the traditional 140/90 mmHg, for the increased prediction of ambulatory hypertension in outpatient, clinical samples; and the cost-effectiveness of the proposed strategy.

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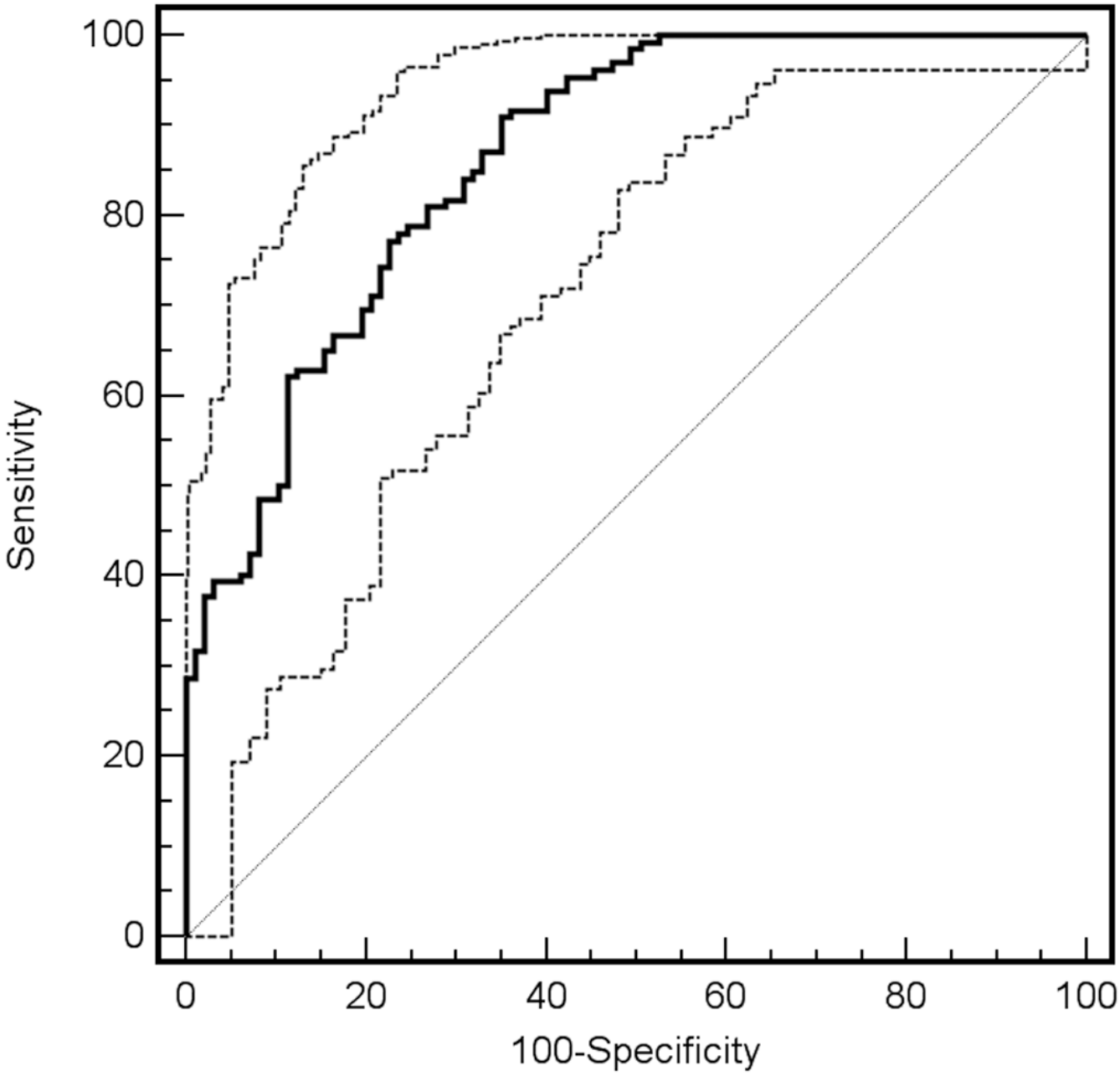

Figure 1.
Receiver-operating-characteristic curve analysis of predictive probabilities based on systolic and diastolic OBP levels to diagnose ambulatory hypertension. Dotted lines represent 95% confidence intervals.

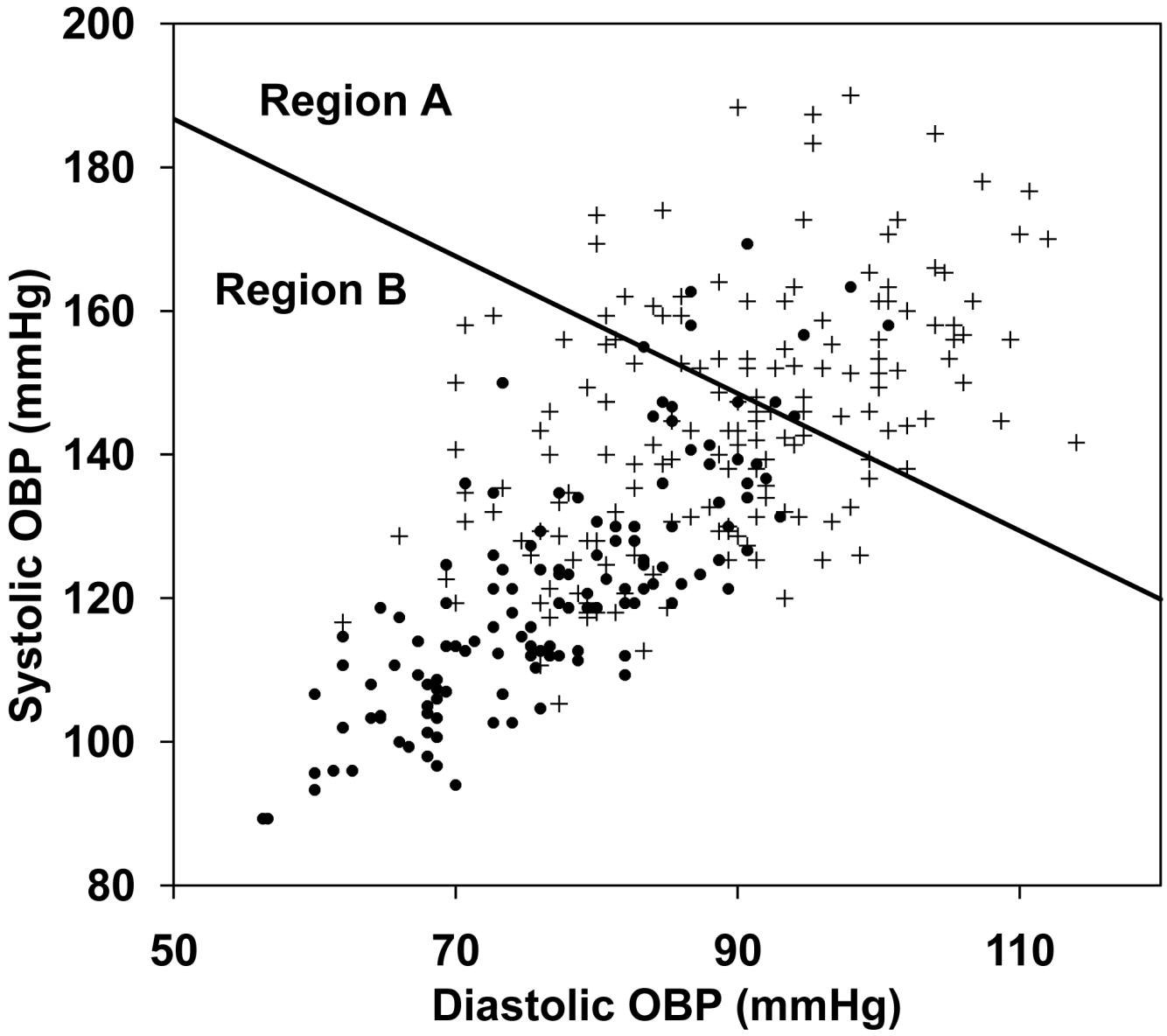

Figure 2.
Scatter plot of systolic and diastolic OBP levels. Region A represents systolic and diastolic OBP levels above the 95% specificity boundary for ambulatory hypertension. Region B represents OBP levels outside of Region A. Solid circles and crosses represent participants with normal ABP levels and participants with ambulatory hypertension respectively.

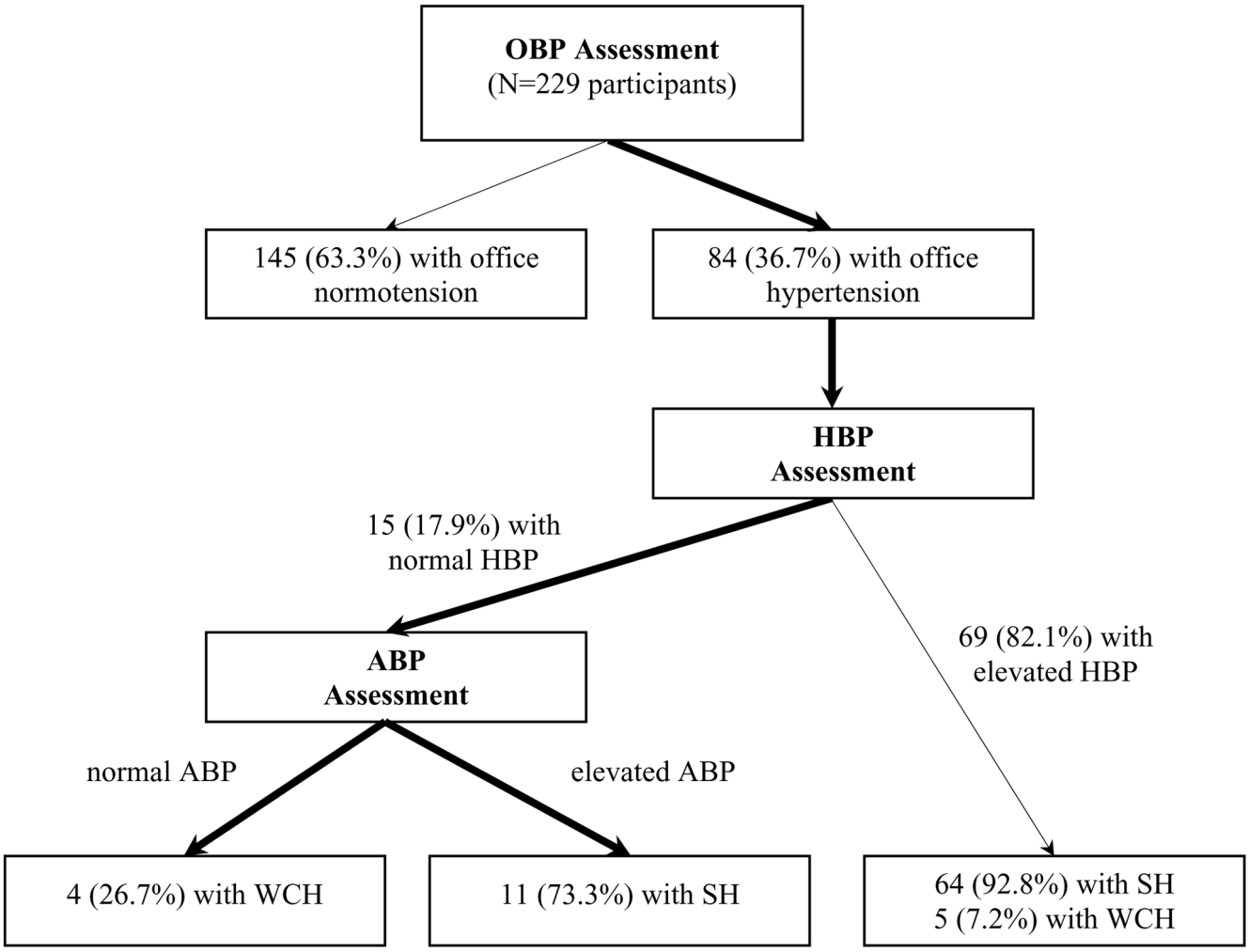

Figure 3.
Flow diagram of original algorithm using OBP and selected HBPM and ABPM to diagnose SH and WCH. Bold lines represent the components of the algorithm. In patients with office hypertension (systolic OBP ≥140 or diastolic OBP ≥90 mmHg, on two occasions), HBPM is initially performed; ABPM is performed only in those with normal HBP levels (SBP <135 and DBP <85 mmHg).

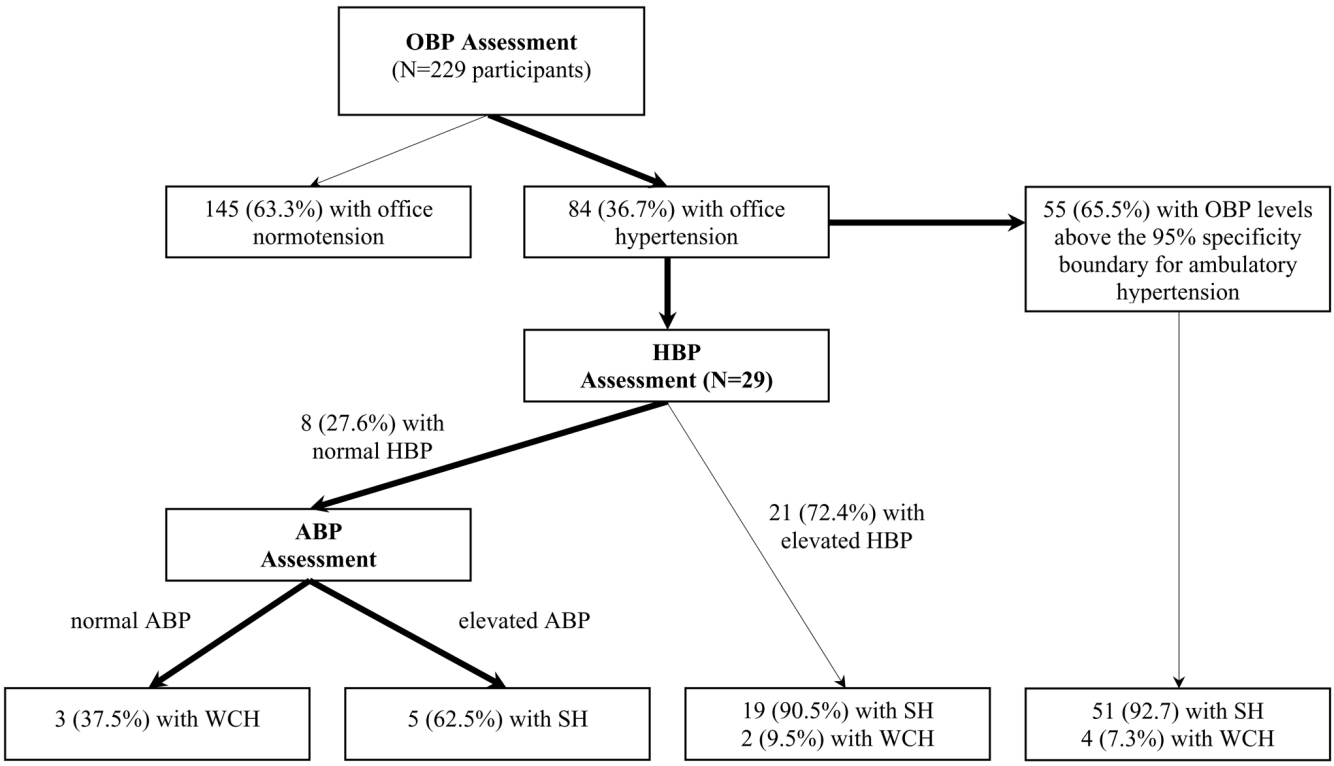

Figure 4.
Flow diagram of modified algorithm incorporating 95% specificity boundary for ambulatory hypertension. Bold lines represent the components of the algorithm.

Table 1

Sample characteristics*

Characteristics		Total Sample (N=229)	
Age, y		52.5 ± 14.6	
Sex, % female		54.1	
Race			
% White (Non-Hispanic)		60.7	
% White (Hispanic)		9.2	
% Black (Non-Hispanic)		17.5	
% Black (Hispanic)		1.7	
% Asian/Indian/Pacific Islander		6.1	
% Native American/Alaskan Native		0.4	
% Other		4.3	
Office	First visit	Second visit	Both visits†
Systolic blood pressure, mmHg	134 ± 21	133 ± 22	133 ± 21
Diastolic blood pressure, mmHg	83 ± 12	83 ± 13	83 ± 12
% Hypertensive‡		36.7	
Ambulatory (awake)			
Systolic blood pressure, mmHg		135 ± 14	
Diastolic blood pressure, mmHg		83 ± 10	
% Hypertensive§		57.6	
Home			
Systolic blood pressure, mmHg		133 ± 18	
Diastolic blood pressure, mmHg		82 ± 11	
% Hypertensive§		56.3	

*Data are expressed as percentage or mean ± SD.

†Average of six OBP measurements (3 from first visit and 3 from second visit)

‡Defined by having a mean systolic blood pressure ≥ 140 or diastolic blood pressure ≥ 90 mmHg on first visit and also second visit.

§Defined by mean systolic blood pressure ≥ 135 or diastolic blood pressure ≥ 85 mmHg.