Relevance to Home Blood Pressure Monitoring Protocol of Blood Pressure Measurements Taken Before First-Morning Micturition and in the Afternoon

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Abstract

Background: The importance of measuring blood pressure before morning micturition and in the afternoon, while working, is yet to be established in relation to the accuracy of home blood pressure monitoring (HBPM).

Objective: To compare two HBPM protocols, considering 24-hour ambulatory blood pressure monitoring (wakefulness ABPM) as gold-standard and measurements taken before morning micturition (BM) and in the afternoon (AM), for the best diagnosis of systemic arterial hypertension (SAH), and their association with prognostic markers.

Methods: After undergoing 24-hour wakefulness ABPM, 158 participants (84 women) were randomized for 3- or 5-day HBPM. Two variations of the 3-day protocol were considered: with measurements taken before morning micturition and in the afternoon (BM+AM); and with post-morning-micturition and evening measurements (PM+EM). All patients underwent echocardiography (for left ventricular hypertrophy - LVH) and urinary albumin measurement (for microalbuminuria - MAU).

Result: Kappa statistic for the diagnosis of SAH between wakefulness-ABPM and standard 3-day HBPM, 3-day HBPM (BM+AM) and (PM+EM), and 5-day HBPM were 0.660, 0.638, 0.348 and 0.387, respectively. The values of sensitivity of (BM+AM) versus (PM+EM) were 82.6% × 71%, respectively, and of specificity, 84.8% × 74%, respectively. The positive and negative predictive values were 69.1% × 40% and 92.2% × 91.2%, respectively. The comparisons of intraclass correlations for the diagnosis of LVH and MAU between (BM+AM) and (PM+EM) were 0.782 × 0.474 and 0.511 × 0.276, respectively.

Conclusions: The 3 day-HBPM protocol including measurements taken before morning micturition and during work in the afternoon showed the best agreement with SAH diagnosis and the best association with prognostic markers. (Arq Bras Cardiol. 2014; 103(4):338-347)

Keywords: Arterial Pressure; Mass Screening; Predictive Value of Tests; Ambulatory Blood Pressure Monitoring; Cardiovascular Diseases/urine; Hypertension.

Introduction

Ambulatory blood pressure monitoring (ABPM) has been recognized as the reference method to predict the cardiovascular risk associated with increased blood pressure (BP). Longitudinal studies with population samples[1-3] and hypertensive individuals[4,5] have reported the better ability of ABPM to stratify risk as compared with measurements taken at the office. More recently, home blood pressure monitoring (HBPM) has been accepted in different guidelines as an effective method to measure usual BP and as a useful tool to stratify cardiovascular risk[6-11]. This low-cost method has potential clinical use in different scenarios, such as in establishing the diagnosis and prognosis of systemic arterial hypertension (SAH), in 'white coat hypertension' and 'masked hypertension', in assessing BP levels of the elderly and hypertensive individuals with diabetes, in resistant hypertension, and in assessing adherence to anti-hypertensive treatment, as a guide for pharmacological interventions[6-9,12-14].

Home blood pressure monitoring is defined as the systematized out-of-office BP measurement by the patient or any skilled person, during wakefulness, following a specific and standardized protocol, which is different from self-blood pressure measurement (SBPM), which is the non-systematized reading performed according to doctor's guidance or patient's decision[7]. European and

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North-American guidelines lack accuracy regarding protocol systematization and control, which can be mistaken for SBPM[8,9,15,16]. However, inconsistencies in protocol recommendations regarding hours, number of days and measurements taken during HBPM are still observed[17-20]. The HBPM protocols of the Brazilian Society of Cardiology (SBC)[7] and of the Japanese Society of Hypertension[6] recommend BP measuring in the morning after micturition, avoiding urinary bladder distension and consequent BP elevation. The influence of BP measurements taken in the afternoon during work on the estimation of usual BP is still arguable[21]. The European Society of Hypertension[15,16] recommends BP measurement for seven days, two taken in the morning and two in the evening, the means of the first day being discarded for the purpose of diagnosis and therapeutic decisions. It is worth noting the lack of major recommendations on the influence of micturition or other conditions on the accuracy of HBPM.

The objective of the present study was to assess the influence on the SAH diagnosis of BP measurements taken immediately after waking up (before micturition) and in the afternoon, considering ABPM during wakefulness as gold-standard. In addition, the secondary objective was to assess the association of prognostic markers, such as microalbuminuaria (MAU) and left ventricular hypertrophy (LVH), with HBPM protocols that differ about the inclusion or exclusion of measurements taken before and after morning micturition or in the afternoon.

Methods

Population

Individuals referred for assessment of ABPM at a private clinic specialized in cardiology in the city of João Pessoa, Paraíba state, were eligible for this study. They were consecutively assessed at medical office, and, after anamnesis and physical examination, the individuals meeting the inclusion criteria were invited to participate in the study and to sign the written informed consent previously approved by the ethics committee of the institution. Patients with the following characteristics were excluded from the study: cardiac arrhythmia; cognitive deficit; and visual deficit hindering the measurements. In addition, exams that did not reach the required number of measurements were excluded from the analysis: < 16 validated measurements during wakefulness and/or < 8 measurements during sleep on ABPM or < 14 validated measurements on HBPM[7].

Study design

This is a diagnostic cross-sectional study to compare different HBPM protocols, considering 24-hour ABPM as gold-standard, for the diagnosis of SAH. All diagnostic tests were performed between February 2009 and April 2010.

Study protocol

The analyses of this investigation complement previously published data. The recruiting flowchart (Figure 1) and the assessment protocols have been previously described (Figure 2)[22]. Briefly, after personal data collection, patients underwent 24-hour ABPM, after which, all were randomized to one of the HBPM protocols (three or five days) and later crossover with a five-day interval between protocols. All patients completing the study underwent both HBPM protocols. For BP measurements, both protocols followed the SBC recommendations, as previously described[15,22].

ABPM protocol: the recommendations for ABPM were in accordance with those of the SBC V guidelines for ABPM[7], with SBP and DBP measurements taken every 15 minutes during wakefulness and every 20 minutes during sleep.

HBPM protocol: for both protocols, in the morning of the first day, patients underwent the first three BP measurements with a trained nurse, and received all instructions about the protocols to be followed at home. The numbers and times of measurements are shown in Figure 2. On the three-day HBPM protocol, up to 33 BP measurements could be obtained, and, on the five-day HBPM protocol, up to 27 measurements. In both protocols, participants were instructed to take three measurements in the presence of any sign or symptom, at any time of the day, and record them on the diary.

To assess the impact of micturition and afternoon measurements on the accuracy of the three-day protocol as compared with that of the five-day protocol, the following sets of measurements were considered:

- three-day HBPM with all measurements (standard three-day HBPM);
- three-day HBPM with measurements taken before morning micturition and in the afternoon (HBPM-BM+AM);
- three-day HBPM with post-morning-micturition and evening measurements (HBPM-PM+EM).

Devices

ABPM: the Spacelabs 90207 monitor (Spacelabs, Washington, DC, United States) validated by the British Hypertension Society was used[23].

HBPM: the validated Microlife BP A 100 Plus device (Microlife, Heerbrugg, Switzerland) was used[24].

Definitions and measurements of major variables

Systemic arterial hypertension assessed with ABPM was defined as systolic blood pressure (SBP) > 130 mmHg and diastolic blood pressure (DBP) > 80 mmHg in 24 hours. For ABPM during wakefulness, those values were SBP > 135 mmHg and DBP > 85 mmHg. For HBPM, the criterion adopted for the diagnosis of SAH was SBP at home > 135 mmHg and DBP at home > 85 mmHg[7]. For ABPM, wakefulness was defined as the time interval between waking up and going to bed, according to records documented in the diary.

Urinary albumin

On the initial exam, urinary albumin concentration, MAU, was measured in a urine sample by using immunoturbidimetric

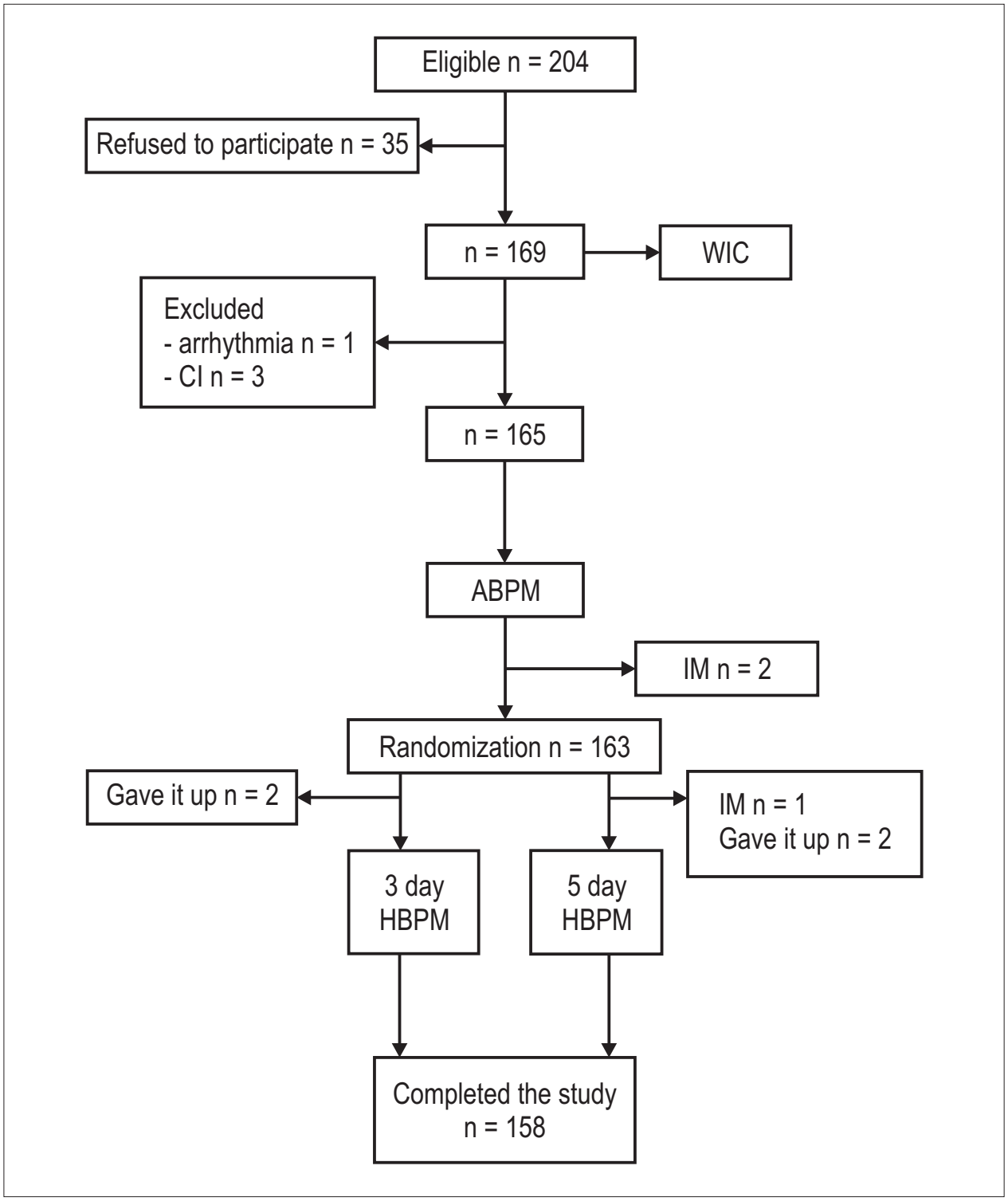

Figure 1 – *Flowchart of population recruitment. IM: insufficient measurements; CI: cognitive impairment; WIC: written informed consent; HBPM: home blood pressure monitoring; ABPM: ambulatory blood pressure monitoring.*

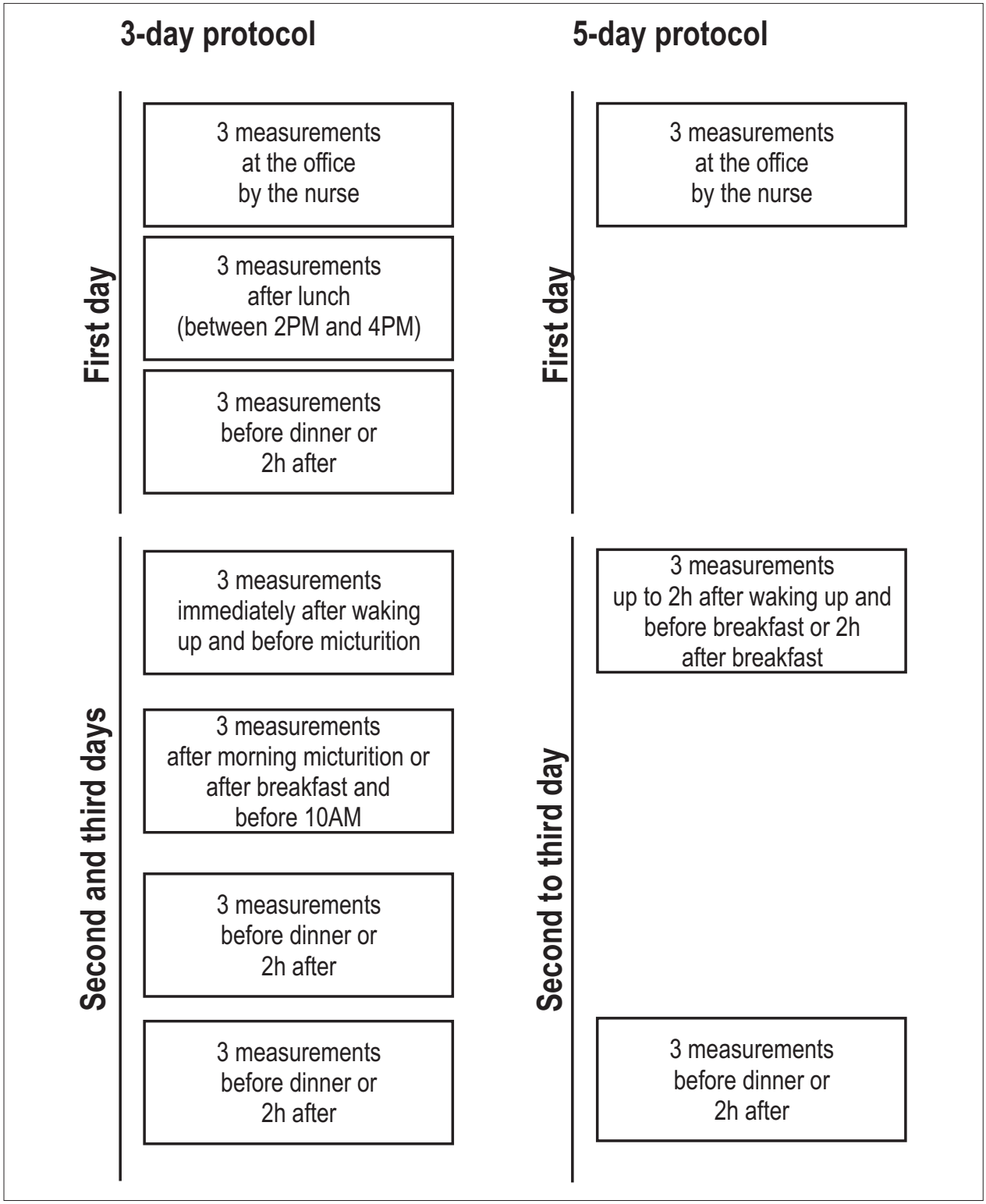

Figure 2 – *Diagram of the protocols of 3-day and 5-day home blood pressure monitoring (HBPM).*

assay (AlbuminLatex, BioSystems S.A., Barcelona, Spain). At our laboratory, the mean intra-assay and interassay coefficients of variation were 2.4% and 5.7%, respectively, the lower limit of detection was 0.9 mg/L, and the cutoff point for the diagnosis of MAU was > 15 mg/L. The MAU determined from a single urine specimen is highly correlated with 24-hour urinary albumin excretion[25-27].

Echocardiography

To assess left ventricular mass (LVM), two-dimensional echocardiography with a Sonosite M-turbo machine (M-turbo Sonosite Inc., Bothell, WA, USA) was used. The measurements were taken according to the American Society of Echocardiography recommendations[28]. The LVM (g) was calculated by using the Devereux equation[29], and the LVM index (LVMI) in this study was defined as LVM (g)/body surface (m^2). The diagnosis criteria for LVH were LVMI values of ≥ 115 g/m^2 and ≥ 95 g/m^2 for men and women, respectively[28,29].

Statistical analysis

All parameters were typed by a single trained examiner and independently of collection into a single database for further analysis. Data were assessed with the IBM SPSS Statistics 19 (IBM Company, USA). The continuous variables were described as mean ± standard deviation. The means of the BPs between the tests were compared by using ANOVA for repeated measures. To assess the impact of drug use in the population, the hierarchical log-linear model with multinomial distribution was used. The area under the Receiver Operating Characteristic (ROC) curve was calculated, and the accuracy of HBPM protocols was described based on sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and positive and negative likelihood ratios (PLR and NLR, respectively) with their respective 95% confidence intervals. Agreement between the diagnosis of SAH established by using ABPM during wakefulness, MAU, LVH and the two three-day HBPM protocols was assessed by use of kappa coefficient, ROC curve and intraclass correlation coefficient. The associations between ABPM and three-day HBPM were presented with the intraclass correlation coefficient, and dispersion and Bland-Altman plots. An alpha error probability < 5% was considered significant.

Results

Of the 204 patients invited to participate in this study, 169 accepted and 158 concluded it (Figure 1)[22]. Those who refused to participate and were excluded from the study had the same characteristics of the population assessed regarding age, sex and body mass index (BMI).

On initial assessment, four patients were excluded, one due to arrhythmia (atrial fibrillation) and three due to cognitive impairment. On ABPM, two patients were excluded due to insufficient number of measurements, because of equipment battery failure. On the three-day HBPM protocol, two patients left the study due to a trip, and, on the five-day HBPM protocol, one patient was excluded because of insufficient measurements (forgot to take BP measurements on the last two days), and two patients were excluded due to a trip. Regarding the patients who concluded all protocols, no change was observed in their lifestyle, medications and usual hours during the study. In the three-day protocol, 24 BP measurements were taken, and, in the five-day protocol, 19 measurements.

Table 1 shows the major characteristics of the population comprised of overweight middle-aged patients with slight predominance of the female sex. Half of them were on anti-hypertensive drugs, ABPM being mainly indicated for SAH diagnosis and treatment. The final diagnoses of 'white coat hypertension' and 'masked hypertension' were established in 18.3% and 3.1% of the patients, respectively. Assessment by using hierarchical log-linear model with multinomial distribution showed no difference regarding the use of drugs ($p = 0.221$). No significant difference in MAU between men and women was found (16 ± 11 mg/L; 14 ± 10 mg/L; $p = 0.121$). The mean LVMI values were 112 ± 15 g/m^2 and 88 ± 9 g/m^2 for men and women, respectively ($p = 0.001$).

Table 2 shows the means of ABPM during wakefulness, standard three-day HBPM, three-day HBPM-BM+AM, three-day HBPM-PM+EM, and five-day HBPM, with significant differences between them for SBP and DBP. Figure 3 shows the dispersion and Bland-Altman plots for SBP and DBP, with smaller dispersion and better agreement of the BM+AM protocol as compared with the PM+EM protocol of the three-day HBPM obtained by associating with ABPM during wakefulness.

Table 3 shows a difference in kappa values between the three-day HBPM protocols when the micturition subject is considered in the analysis. Table 4 shows better diagnosis accuracy for the standard three-day HBPM and three-day HBPM-BM+AM protocols, considering ABPM during wakefulness as gold-standard. Table 5 shows that, using the cutoff points previously defined for the diagnosis of SAH and considering all forms of ambulatory measurements, the standard three-day HBPM protocol, the three-day HBPM-BM+AM protocol and the ABPM during wakefulness protocol had the best agreement and correlated better with the diagnosis of MAU and LVH.

Discussion

The major finding in this study was that, considering ABPM during wakefulness as gold-standard for the diagnosis of SAH, the HBPM protocol including BP measurements taken before the first morning micturition and in the afternoon had the best accuracy to diagnose SAH as compared with the other protocols assessed. In addition, that three-day HBPM protocol performed better than the longer five-day protocol, thus being useful and having a practical potential to the routine assessment of hypertensive individuals. Furthermore, that strategy correlates better with prognostic markers, such as MAU and LVH. Because of the clinical relevance of that finding, three-day HBPM protocols should include measurements taken before morning micturition and in the afternoon.

Studies considering the importance of micturition for HBPM accuracy lack in the literature. The SBC guidelines[7,15] on that investigation method recommend BP measurement in the morning after micturition. However, such recommendation is not supported by any scientific reference, being thus empirical. The Japanese Society of Hypertension guideline[6] makes the same recommendation, based on one single Japanese study published as an abstract and showing BP elevation associated with morning urinary bladder distension. In defining the HBPM protocol, the European[15,30] and North-American[9] guidelines make no reference to that subject.

In addition, the circadian variation of BP depends on three major factors: physical activity, autonomic function and sodium sensitivity[31]. Fagius and Karhuvaara[32] have shown an association between BP elevation and urinary bladder distension in 16 healthy individuals after fluid ingestion. That finding has been justified by the vesicovascular stimulus related to an increase in sympathetic flow, which is mediated by vasoconstrictor neurons, thus increasing BP. Scott et al[33] have shown that, in healthy individuals, the BP elevation that follows water ingestion is associated with increases in serum norepinephrine levels, in sympathetic activity and in peripheral vascular resistance. Callegaro et al[34], studying normotensive and hypertensive individuals, have reported that the BP increase after acute water ingestion could be explained by an increased vasoconstrictor sympathetic activity. Studies assessing cold exposure[35] and mental stress exposure[36] have also reported BP elevation due to sympathetic activity. All those factors can be considered as part of the BP circadian cycle complex, and there is convincing evidence that it plays an important role in BP variability regulation[37]. Thus, those questions should be assessed at the time the accuracy of BP measuring tests is assessed for a prolonged time or of proposed HBPM protocols. Thus, by discriminating BP in a more reliable way, the diagnosis and treatment of SAH can be better established, and target-organ lesions prevented in the long run. In that scenario, adding measurements to the standard HBPM, considering first-morning micturition and stress at workplace, can influence the accuracy of the method for SAH diagnosis.

The number of measurements of HBPM should be considered, although the optimal number to be used remains controversial in the different guidelines[6-9,11,15,16]. Garcia-Vera and Sanz[21] have assessed HBPM in 43 treated hypertensive patients. In their study, two BP measurements were taken in the morning, in the afternoon during work, and in the evening. That procedure was repeated after one and six months. The results have shown that two measurements would suffice, one at the workplace and the other at home, on three consecutive days, to obtain reliable BP estimates. Another finding from that study is that BP measurements at the workplace were consistently higher than those obtained at home. Kario et al[38] have assessed the influence of work-and home-related stress on sympathetic activation and BP in 134 women. Those authors have shown that work-related stress increased BP levels throughout the day, and the home-related stress induced an additional sympathetic activation. Those data corroborate our protocol, which includes one measurement in the afternoon during work, which better correlated with the diagnosis of SAH.

Den Hond et al[39], studying 247 patients, have compared HBPM with ABPM during wakefulness (SAH ≥ 135/85 mmHg) by using a protocol with three measurements taken in the morning and evening for seven days. They have found sensitivity,

Table 1 – Characteristics of the population (n = 158)

Parameters assessed	Total sample n = 158
Age (years)	50.6 ± 13.5
Male sex	74 (46.8)
BMI (kg/m^2)	28.3 ± 4.9
Use of anti-hypertensive drugs	80 (50.6)
Office measurement SBP (mmHg)	130 ± 14.0
Office measurement DBP (mmHg)	80.7 ± 10.1
Indication for BP monitoring	
Hypertension	117 (74.1)
White-coat hypertension	32 (20.3)
Masked hypertension	9 (5.7)

Results shown as mean ± SD or n (%).
BMI: body mass index; BP: blood pressure; DBP: diastolic blood pressure; SBP: systolic blood pressure.

Table 2 – Mean ± SD of systolic blood pressure (SBP) and diastolic blood pressure (DBP) of ambulatory blood pressure monitoring (ABPM) and of the different HBPM protocols

	SBP	ANOVA p	DBP	ANOVA p
Wakefulness ABPM	128.5 ± 14.1		79.7 ± 10.4	
Standard 3-day HBPM	126.1 ± 13.8		78.2 ± 9.8	
3-day HBPM-BM+AM	127.4 ± 14.1	0.001	79.5 ± 10.2	0.001
3-day HBPM-PM+EM	124.8 ± 13.6		76.8 ± 9.7	
5-day HBPM	126.1 ± 13.3		78.3 ± 10.4	

HBPM: home blood pressure monitoring; BM+AM: *measurements taken before morning micturition and in the afternoon; PM+EM: measurements taken post morning micturition and in the evening.*

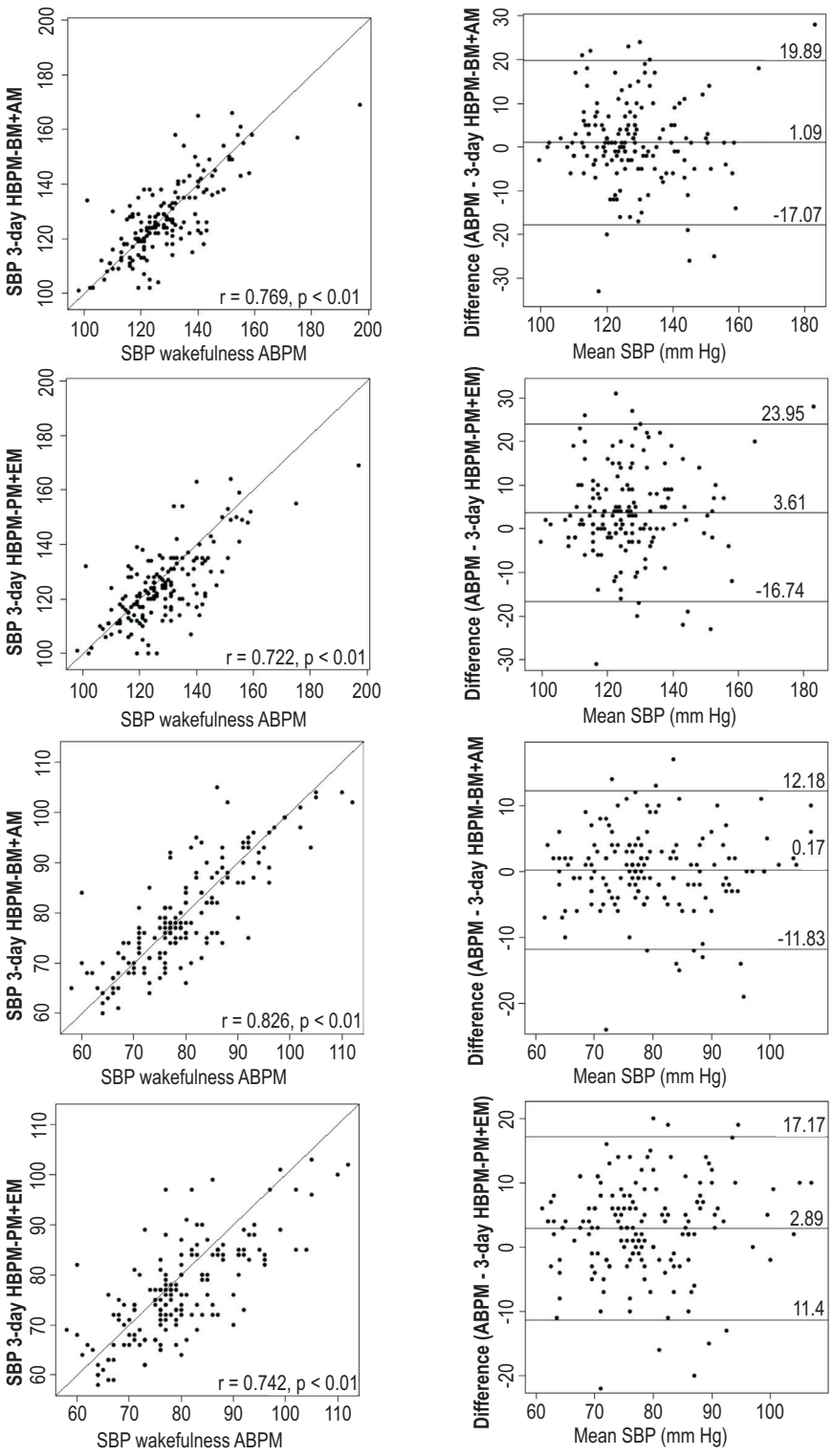

Figure 3 – *Dispersion and Bland-Altman plots of blood pressure measurements comparing 3-day home blood pressure monitoring (HBPM) with ambulatory blood pressure monitoring (ABPM).*
BM+AM: *measurements taken before morning micturition and in the afternoon; PM+EM: measurements taken post morning micturition and in the evening; DBP: diastolic blood pressure; SBP: systolic blood pressure.*

Table 3 – Kappa statistic for the diagnosis of hypertension considering ambulatory blood pressure monitoring (ABPM) during wakefulness as gold-standard

HBPM	Hypertension	3-day BM+AM		3-day PM+EM		Standard 3-day		5-day HBPM	
		No	Yes	No	Yes	No	Yes	No	Yes
Wakefulness ABPM	No	95	8	94	9	93	10	84	19
	Yes	17	38	33	22	14	41	24	31
Kappa		0.638		0.348		0.660		0.387	

HBPM: home blood pressure monitoring; BM+AM: *measurements taken before morning micturition and in the afternoon; PM+EM: measurements taken post morning micturition and in the evening. p < 0.001 for comparison between each protocol and the gold-standard protocol.*

Table 4 – Accuracy of home blood pressure monitoring (HBPM) protocols considering ambulatory blood pressure monitoring (ABPM) during wakefulness as gold-standard

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Positive predictive value (%) (95% CI)	Negative predictive value (%) (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Area under the ROC curve (95% CI)
3-day HBPM BM+AM	82.6 76.5-88.6	84.8 79.1-90.5	69.1 61.7-76.4	92.2 87.9-96.5	5.44 2.79-10.6	0.20 0.13-0.32	0.87 0.72-0.88
3-day HBPM PM+EM	71.0 63.7-78.1	74.0 67.0-81.0	40.0 32.2-47.7	91.2 86.7-95.7	2.73 1.47-5.28	0.39 0.28-0.53	0.72 0.62-0.83
Standard 3-day HBPM	80.4 74.1-86.7	86.9 81.6-92.3	74.5 67.6-81.5	90.3 85.6-95.0	6.14 3.35-9.75	0.23 0.14-0.36	0.82 0.75-0.90
5-day HBPM	62.0 54.3-69.7	77.8 71.2-84.4	56.4 48.5-64.2	81.6 75.4-87.7	2.79 1.75-2.80	0.52 0.38-0.71	0.69 0.60-0.78

BM+AM: *measurements taken before morning micturition and in the afternoon; PM+EM: measurements taken post morning micturition and in the evening; CI: confidence interval.*

Table 5 - Agreement and correlation between the diagnosis of hypertension and the diagnosis of microalbuminuria and left ventricular hypertrophy

Diagnosis	Measurements	Standard 3-day HBPM	3-day HBPM BM+AM	3-day HBPM PM+EM	5-day HBPM	Wakefulness ABPM
MAU	Kappa	0.352	0.342	0.159	0.207	0.372
	ROC curve (95% CI)	0.694 0.594-0.794	0.681 0.579-0.784	0.574 0.466-0.682	0.613 0.508-0.718	0.711 0.614-0.809
	Intraclass correlation (95% CI)	0.526 0.352-0.654	0.511 0.331-0.643	0.276 0.009-0.471	0.346 0.105-0.523	0.552 0.386-0.673
LVH	*Kappa*	0.636	0.641	0.299	0.298	0.587
	ROC curve (95% CI)	0.820 0.742-0.898	0.814 0.733-0.894	0.634 0.536-0.733	0.649 0.533-0.744	0.801 0.722-0.881
	Intraclass correlation (95% CI)	0.778 0.696-0.838	0.782 0.702-0.841	0.474 0.281-0.616	0.459 0.259-0.605	0.741 0.645-0.811

HBPM: home blood pressure monitoring; ABPM: ambulatory blood pressure monitoring; BM+AM: *measurements taken before morning micturition and in the afternoon; PM+EM: measurements taken post morning micturition and in the evening MAU: microalbuminuria; LVH: left ventricular hypertrophy; CI: confidence interval.*

specificity, PPV, NPV and kappa statistic of 68.4%, 88.6%, 33.3%, 97.1% and 0.380, respectively. Comparing their findings with ours originating from the three-day HBPM-BM+AM protocol, theirs have a greater number of measurements taken during the day. However, the results indicate that our protocol performed better, evidencing that not only the number of measurements can influence the accuracy of different protocols, but the time such measurements are taken should be considered.

Limitations

First, ABPM during wakefulness was considered gold-standard for the diagnosis of SAH. It is worth noting that the standard reference to define the best HBPM protocol should be the occurrence of clinical outcomes assessed on longitudinal studies. However, some studies, such as the PAMELA[40] and FINN-Home[41] studies, have also used ABPM as gold-standard. Second, our three-day HBPM protocol had a higher number of measurements

per day as compared with the five-day HBPM protocol. Thus, our results may be a mere consequence of approximation bias. Nevertheless, data clearly showed that the three-day HBPM protocol was better than the five-day HBPM protocol, and that measurements taken at different times had a significant importance to the result, suggesting it should be preferred in clinical practice. The feasibility and efficacy of a HBPM protocol with a greater number of measurements require better assessment in longitudinal studies.

Conclusion

The three-day HBPM protocol comprising measurements taken before first-morning micturition and in the afternoon has better agreement with the diagnosis of SAH, considering 24-hour ABPM as gold-standard, and associates better with prognostic markers as compared with the five-day HBPM protocol.

Author contributions

Conception and design of the research: Almeida AEM, Stein R, Gus M, Fuchs FD, Ribeiro JP; Acquisition of data: Almeida AEM, Arévalo JRG; Analysis and interpretation of the data: Almeida AEM, Stein R, Gus M, Nascimento JA, Belli KC, Arévalo JRG, Ribeiro JP; Statistical analysis: Almeida AEM, Stein R, Nascimento JA, Ribeiro JP; Obtaining financing: Stein R, Gus M, Fuchs FD; Writing of the manuscript: Almeida AEM, Stein R, Gus M, Nascimento JA, Belli KC, Fuchs FD, Ribeiro JP; Critical revision of the manuscript for intellectual content: Almeida AEM, Stein R, Gus M, Belli KC, Arévalo JRG, Fuchs FD, Ribeiro JP.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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