The accuracy of GP blood pressure measurements …

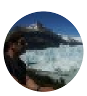
ARTICLE · JUNE 2014

DOI: 10.3132/pccj.2014.022

3 AUTHORS:

Airton T Stein
Universidade Federal de Ciências da Saúde d…

Lúcia Pellanda
Fundação Universitária de Cardiologia (FUC)



Guilherme Brasil Grezzana
Fundação Universitária de Cardiologia (FUC)

Prim Care Cardiovasc J 2014;7:71-75. doi:10.3132/pccj.2014.022

The accuracy of GP blood pressure measurements compared with 24-hour ambulatory monitoring

Guilherme Brasil Grezzana*
PhD student at Instituto de Cardiologia do Rio Grande do Sul (ICFUC) and MSc in Cardiology at Instituto de Cardiologia do Rio Grande do Sul (ICFUC).

Airton Tetelbon Stein
Full Professor – Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA) and Universidade Luterana do Brasil (ULBRA) and Coordinator of HTA of Conceição Hospital

Lucia Campos Pellanda
Associate Professor – Instituto de Cardiologia do Rio Grande do Sul (ICFUC) and Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA).

*Corresponding author:
Guilherme Brasil Grezzana
Clínica Del Cuore de Cardiologia,
Oswaldo Hampe Street, 254,
Antônio Prado, RS, Brazil 95250000

Email: gbgrezzana@yahoo.com.br

We evaluated the accuracy and predictive value of conventional blood pressure (BP) measurements performed by primary care physicians in comparison with ambulatory blood pressure monitoring (ABPM) in a cross-sectional study of hypertensive patients in primary healthcare. We found that conventional BP measurements are less accurate than 24-hour ABPM.

POINTS FOR THE CLINIC

- Conventional blood pressure measurements were less accurate than ABPM
- Blood pressure control was poor in many patients
- Nearly one-third of patients had white coat hypertension
- One-eighth of patients had masked hypertension

INTRODUCTION

Systemic arterial hypertension (SAH) represents the most important single risk factor for premature mortality worldwide[1] and is the main modifiable risk factor for cardiovascular disease (CVD),[2,3] estimated to cause approximately 7.6 million deaths every year.[4] High blood pressure is the leading risk factor for burden (7%; 95% CI 6.2 – 7.7%) of global disability-adjusted life-years (DALYs), the sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.[5] Blood pressure (BP) control remains poor in most patients who have pharmacological treatment,[3] with only 10% of the hypertensive patients in our local population reaching therapeutic goals.[6] GPs have an important role in achieving BP control for their patients, but their results are mostly based on conventional BP measurements, and these are often unsatisfactory.[7]

ABPM may predict mortality, cardiovascular morbidity and end-stage renal disease more accurately than conventional measurements performed by the physician and some recent guidelines recommend ABPM for diagnosis and assessing control,[8] but it has not been widely utilised in primary healthcare to evaluate the effectiveness of antihypertensive treatment.[9,10] ABPM provides an opportunity to refine strategies of risk stratification.[11] It allows circadian variability[12,13] and night-time systolic pressure to be evaluated; the latter is a stronger predictor of cardiovascular events than daytime systolic pressure in hypertensive patients from different populations.[14]

The objective of this study was to evaluate the accuracy of conventional BP measurements in hypertensive patients, performed by primary care physicians with the aid of a sphygmomanometer, when compared with ABPM in a primary healthcare setting.

METHODS

Participants

The participants in this cross-sectional study were enrolled between January 2009 and December 2012 in Antônio Prado (RS), a town in Southern Brazil with a total population of 12,837 inhabitants.[13] They were hypertensive patients over 18 years old who had been using antihypertensive drugs for the past three months. All patients were enrolled in the Family Health Programme (Programa de Saúde da Família) local health centres, the country's Public Health System that provides care for 54.6% of the city's population, and Programa Hiperdia (a federal registry targeting hypertensive patients). Between January 2009 and December 2010, some 146 out of 618 hypertensive patients registered on the family health programme in the city's two health centres were randomly selected. Three patients who did not complete the protocol with ABPM were subsequently lost to follow-up.

Patients who were not able to reply to the questionnaire, pregnant women, individuals not in sinus rhythm according to their ECG and people who lived outside the area covered by the local health centres were excluded. Each study participant provided informed consent. The blood samples were taken by a trained nurse in a period outside the BP measurement period and had no influence on the BP measurements. The study was given approval by the institutional Committee of Ethics in Research.

Conventional BP measurement

There were seven primary healthcare physicians involved (the total number of GPs who treated adult patients in the public health system). They were instructed to perform three BP measurements with a mercury sphygmomanometer using a correctly-sized cuff (a special size cuff was used for obese patients), with the patient seated after five minutes of rest. The GPs were instructed to perform the measurements in both arms, taking as the reference BP the highest BP value after an interval of three minutes between each measurement. The first measurement was excluded and the average of the following two measurements was obtained. After that, in the same visit, the patient was evaluated by a nurse trained in the procedures for this study: she was responsible for administering the questionnaire, performing the 12-lead electrocardiogram and applying ABPM during a patient's typical day.

Blood pressure monitoring and measurements

Monitors that were properly validated and calibrated (DMS Brazil model TM 2430) and approved by the British Hypertension Society were applied.[15] 24-hour ABPM measurements were performed every 15 minutes while the patient was awake and every 30 minutes during sleep, and they were adjusted once the patient answered questions about their usual times of sleeping and waking. Data originated from a minimum of 70 records throughout over 24 hours: those with at least two readings every hour during the night were considered adequate. The parameters evaluated by ABPM were: average systolic and diastolic BP in 24 hours, and systolic and diastolic BP while the patient was awake and during the night. Hypertension through conventional measurements, using a sphygmomanometer, was defined as BP equal to or higher than 140/90 mmHg. ABPM results were considered the gold standard and were analysed blind by one of the authors (GBG) in comparison with conventional BP measurements (index test). The ABPM criteria for poorly controlled hypertension were defined as average 24-hour BP values above 130/80 mmHg. For the values related to the period of wakefulness, uncontrolled BP was considered as an average above 130/85 mmHg.

The absence of nocturnal dipping was defined as a reduction of BP according to ABPM measurements less than or equal to 10% of the diurnal average. White coat hypertension (WCH) was defined as the condition in which BP is elevated when measured in a physician's office, although controlled in other situations.[6] Current clinical guidelines do not present clear cut-off values for the criteria used to define normality regarding 24-hour BP and, thus, values were taken to be the same among diabetic and non-diabetic patients.

Table 1: Descriptive characteristics of the study population

Variables	Numbers, percentages, mean (range)
Demographic variables	
Number of patients	143
Female	96 (67%)
Age (years)	59.8 (29 – 89)
White	113 (79.6%)
Diabetic	30 (21%)
Inflammatory markers	
Hs-CRP > 3 (mg/dL)	59 (41.3%)
Fibrinogen > 400 (mg/dL)	42 (29.37%)
Metabolic descriptors	
Glycosylated haemoglobin (%)	6.19 (4.4-13.14)
Fasting glucose (mg/dL)	101 (53-282)
Microalbuminuria (mg/g creatinine)	91.9 (1.3-3471)
Lipid variables	
Total cholesterol (mg/dl)	212.55 (125-362)
HDL-C (mg/dL)	49.15 (22-91)
LDL-C (mg/dL)	130.7 (55-265)
Triglycerides (mg/dL)	164.13 (50-626)
Anthropometric data	
BMI, kg/m^2	27.98 (19.8-47.9)
Normal weight	30.5%
Overweight	36.9%
Obese	32.6%
Waist-hip ratio	1.52
Lifestyle	
Smokers	13 (9.2%)
Alcohol use >5 units per day	23 (16.1%)

Key: HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; BMI=body mass index; hs-CRP=high-sensitivity C-reactive protein

Clinical charts were reviewed for additional clinical data. Biochemical tests included: lipid profile, creatinine, potassium, high-sensitivity C-reactive protein (hs-CRP), fibrinogen, complete blood count, haemoglobin A_{1c}, microalbuminuria and glycaemia. Clinical examination included: weight, height, body mass index, waist-hip ratio and smoking and/or alcohol status.

Statistical methods

The analysis of data was performed using the statistical program SPSS 17.0. Descriptive statistics were derived for continuous and categorical data, as well as estimation of pre-test probability, sensitivity, specificity and predictive value with 95% confidence intervals for conventional BP measurements (the index test) in comparison with ABPM (the reference test). Risk factors and cardiovascular disease frequencies were described. Kappa statistics was used to evaluate agreement between techniques.

A sample size of 142 patients was estimated, considering a probability of BP control of 30% and 10% with ABPM and conventional measurements, respectively, a 95% confidence interval and statistical power of 80%.

Table 2: BP measurement results using ABPM and BP measured by physicians. Values given are for controlled BP.

BP measurements	Number (percentage)
ABPM measurements	
Systolic 24h, mmHg	128 (96-166)
Diastolic 24h, mmHg	75.8 (58 – 99)
Dipper	40 (28%)
Non-dipper	103 (72%)
24-hour BP control	79 (55.2%)
Uncontrolled while awake	60 (42%)
Poor control	64 (44.8%)
Office measurements	
Systolic, mmHg	143.69 (90-220)
Diastolic, mmHg	85.83 (60-120)
Controlled BP	59 (41.3%)
Systolic BP controlled	56 (39.2%)
Diastolic BP controlled	89 (62.2%)
Uncontrolled	84 (58.7%)

RESULTS

Patients were predominantly female (67%) and white (79.6%), with an average age of 59.8 years. Twenty-one percent had diabetes, 63.6% had high cholesterol (> 5.18 mmol/l), 9.2% were smokers, 16.1% reported drinking regularly and 32.6% were obese (Table 1). Seventy-nine patients (55.2%) were considered to have achieved BP control (<130/80 mmHg), according to 24-hour ABPM measurement, 64 (44.8%) were poorly controlled (>130/80 mmHg), 103 (72%) did not have BP nocturnal dipping, and 60 (42%) had uncontrolled BP while awake (Table 2). When the BP measurements performed by primary care physicians were evaluated, 59 patients (41.3%) with controlled BP (<140/90 mmHg) and 84

Figure 1: Flow diagram showing blood pressure control for the patients in this study

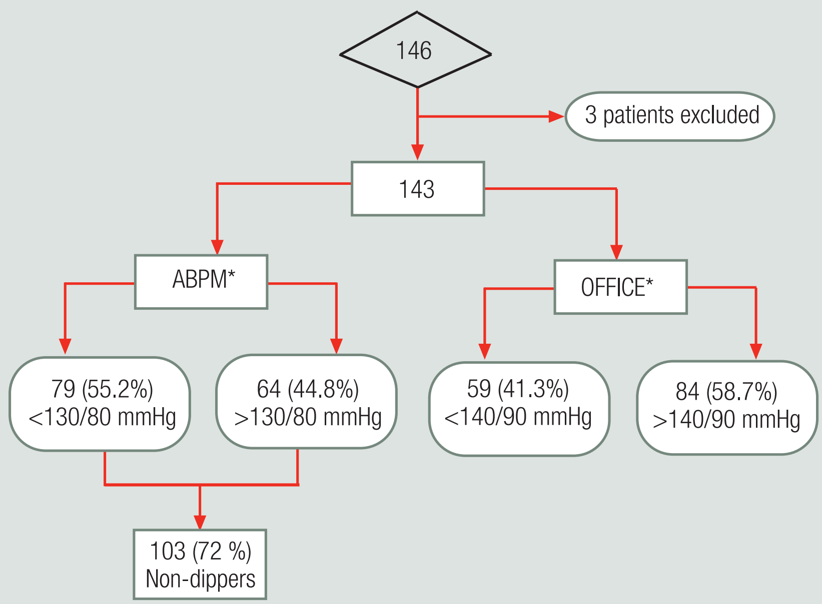


Figure 2: ROC curve for systolic pressure in office vs ABPM

Figure 2a: Plotting systolic pressure and ABPM

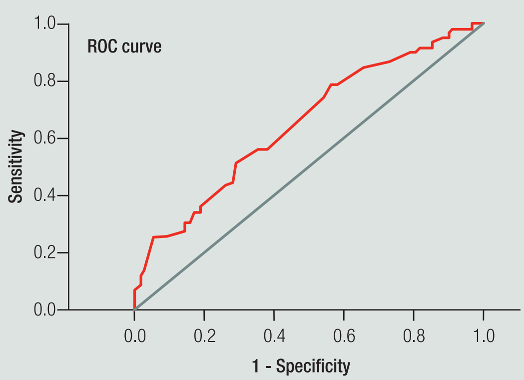
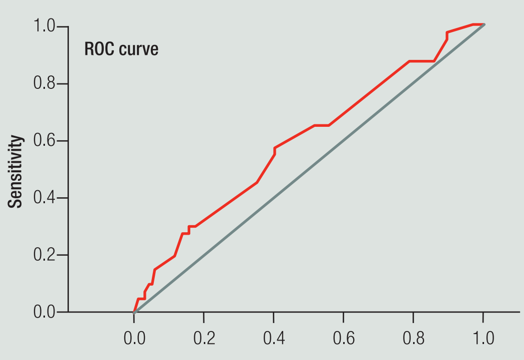


Figure 2b: Plotting diastolic pressure and ABPM

Diagonal segments are produced by ties
ROC curve for diastolic pressure



patients (58.7%) with uncontrolled BP (> 140/90 mmHg) were identified (Figure 1). Using ABPM as the reference or standard test, SBP measured by the GP showed a sensitivity of 0.729 (95% CI 0.625 – 0.820) and a specificity of 0.476 (95% CI 0.403 – 0.540) in detecting high blood pressure. The concordance between measurements made by the physician and ABPM regarding clinical classification as controlled/poorly controlled gave a kappa value of 0.191 for SBP and 0.09 for DBP (Figure 2). In the comparison of DBP measured by the GP in relation to the average 24-hour ABPM, a sensitivity of 0.450 (95% CI 0.314 – 0.598) and a specificity of 0.65 (95% CI 0.598 – 0.704) were obtained.

The measurements of all physicians showed a positive likelihood ratio of 1.391 (95% CI 1.048 – 1.782) and a negative likelihood ratio of 0.569 (95% CI 0.334 – 0.929). The likelihood ratio for a test result compares the likelihood of that result in patients with disease to the likelihood of that result in patients without disease. For DBP, positive likelihood ratio was 1.288 (CI 0.779 – 1.993) and negative likelihood ratio was 0.846 (95% CI 0.583 – 1.149). Positive post-test probability for BP, taking into consideration values of 140/90 mmHg and ABPM as reference test, was 51.2%, and negative post-test probability was 64.4%, Post-test probability, the proportion of cases identified by a test that are true cases, calculated as the number of true positives divided by the number of true positives plus false-positives. When the subgroups were considered, use of alcohol (91.7%), smoking (88.9%) and age over 65 (77.8%) presented the highest values of positive post-test probability, and hs-CRP between 1-3 mg/dL (36.4%), overweight (35.7%) and age over 65 (37%) presented the lowest values of negative post-test probability (Table 3). Forty-two patients (29.37%) showed high blood pressure according to physicians' measurements but normal values according to ABPM and were considered to have the white coat effect. Additionally, 12.58% of the patients had controlled BP as measured by the physician but an abnormal average ABPM during wakefulness, which indicates masked hypertension (MH) (Table 4).

DISCUSSION

The present study evaluated hypertensive patients in a primary healthcare context, utilising ABPM as a standard test, in order to analyse the accuracy of conventionally performed BP measurements. A weak concordance was identified between the two methods of obtaining BP. Moreover, high prevalence of WCH, MH and patients without nocturnal dipping of BP was observed. The highest positive post-test probabilities were observed in patients older than 65 years and those who reported regular alcohol drinking and smoking, and the lowest negative post-test probabilities were observed in patients with hs-CRP between 1-3 mg/dL, overweight and aged over 65.

The main findings of the present study were the low accuracy of conventional BP measurements performed by GPs when compared with 24-hour ABPM and the large number of patients with non-controlled BP. In an Italian study[16] a low accuracy of BP measured by physicians in primary healthcare was also observed. These findings are clinically relevant, since

Table 3: Distribution of positive post-test probability and negative post-test probability of BP measurements by the physician in each subgroup using 24-hour ABPM as the reference test.

Factor	Level	PTP + *	PTP - **
All patients		51.2%	64.4%
Age	Under 55 years old	62.5%	48%
	55 – 64 years old	53.8%	59.3%
	Above 65 years old	77.8%	37%
Smoker	Yes	88.9%	100%
	No	63.6%	50%
Gender	Female	69.4%	45%
	Male	64.3%	57.9%
DM		62%	44.4%
BMI > 30 kg/m^2	> 30	81%	48%
	> 25	66.7%	35.7%
	< 25	52.6%	58.3%
Hypercholesterolaemia		74.4%	44.2%
Hypertriglyceridaemia		55%	54.1%
Use of alcohol	Yes	91.7%	36.6%
	No	61.8%	45.6%
CRP	> 3	63.6%	45.9%
	1 - 3	65.5%	36.4%
	< 1	76.9%	65%
Fibrinogen > 400 mg/dL		71%	66.7%

Key: *Positive post-test probability; **Negative post-test probability; DM = diabetes; BMI = body mass index; CRP = C-reactive protein

Table 4: Number of patients with white coat hypertension and masked hypertension (Chi-squared analysis)

	Office	ABPM Waking hours	Total
White coat hypertension	84 (≥ 140/90 mmHg)	42 (<130/85 mmHg)	29.37%
Masked hypertension	59 (<140/90 mmHg)	18 (>130/85 mmHg)	12.58%

misclassification regarding SAH control may lead to incorrect management[4] but studies in primary care settings are still scarce. In clinical practice, it is possible that a large number of hypertensive patients remain insufficiently treated, with low utilisation of antihypertensive medication.[7] However, the amplitude of this difference could be reduced with an increased number of clinic BP readings, to reduce the magnitude of the white coat effect and neutralise regression to the mean.[17]

In this study, we assumed that ABPM measurements are more valid and reproducible and their values more strongly correlated to target organ damage than BP measured by the physician. Consequently, ABPM would show higher prognostic relevance.[17] Previous studies have shown that BP measured by the physician is higher than average levels of 24-hour ABPM. This difference may also be observed when the response to antihypertensive treatment is evaluated.[18,19] The present study shows similar results, with better control of BP when evaluated by ABPM compared with measurements performed by the physician. In a sub-study of Syst-Eur,[18] ABPM was able to discriminate which hypertensive patients had higher cardiovascular risk, according to pressure measurements during the period of wakefulness. Moreover, results from the PIUMA study[13] suggested that hypertensive patients who were controlled according to ABPM would have lower cardiovascular risk, independently of other associated risk factors. Casual BP measurements correlate less well with cardiovascular risk,[20] mainly due to the inaccuracy in measuring 24-hour pressure variability, which is a better predictor of cardiovascular events.[1,11,21,22-23] In people over 60 years old, the majority of individuals involved in this study, elevated SBP indicates a higher absolute risk of cardiovascular events.[22,24]

In the present study, 29.4% of patients had white coat hypertension, 12.6% had masked hypertension and a large number of patients did not have nocturnal dipping of BP (72%). These figures compare well with findings from two other studies, which showed a prevalence of attenuation or absence of nocturnal dipping of BP of 67.5% and 60%, respectively.[24,19] In a recent systematic review,[14] nocturnal systolic pressure was shown to have better predictive value for cardiovascular events than diurnal systolic pressure in hypertensive patients, and in randomly selected individuals from several populations.[25] Thus, hypertensive patients who do not have nocturnal dipping of BP require a more strict adjustment of BP values.[26] This could be one of the focuses of intervention to combat the low effectiveness of antihypertensive treatment seen in the patients included in this study. There is a need to readjust antihypertensive treatment in these patients.

In a systematic review that evaluated the prevalence of masked hypertension,[10] the number of patients with controlled BP measured by the physician and uncontrolled BP measured with subsequent ABPM varied between 9% and 23%. Patients with MH presented a higher cardiovascular risk when compared with normotensive patients.

The prevalence of white coat hypertension is described as approximately 20% of those patients considered to have hypertension based on conventional BP measurements.[27] We found a higher prevalence of 29.37%. This finding was somewhat unexpected,[15] because the hypertensive patients in our sample were followed personally by the same GP who measured BP for the study in the primary healthcare setting; we assumed that since these patients would be acquainted with these professionals they would have a lower "alerting response".[23] This finding is relevant because white coat hypertension is considered to be an intermediate situation between normotension and sustained hypertension and may not be a benign cardiovascular condition.[28]

The patients who drank alcohol, smoked and were aged over 65 obtained the highest positive post-test probability, whereas those with hs-CRP between 1-3 mg/dL, who were overweight and aged over 65 presented the lowest values for negative post-test probability. In a study developed in order to stratify subgroups with higher cardiovascular risk in whom the utilisation of ABPM would be beneficial in the adjustment of BP treatment,[7] low predictive values of BP measured by the physician with male patients, patients with diabetes, those aged over 65, those who used alcohol and were overweight were observed. This would be an interesting strategy to improve the utilisation of 24-hour ABPM in patients considered as controlled by their GPs, without the need to extend this examination to all hypertensive patients. Clinical information obtained with these measurements could have a considerable impact related to cost and effectiveness when properly applied.[17] However, this strategy would need to be validated in a large population of hypertensive patients.

One possible limitation of our study was that only one 24-hour ABPM measurement was taken, which limits the classification into dippers and non-dippers. Repeated ABPM recordings would provide a more accurate classification of circadian patterns, but this approach is not feasible in primary healthcare. However, ABPM was employed with strict protocol measures and considered individualised sleep and wakefulness periods. Another limitation is that this study had an observation design: a Randomised Controlled Trial is essential to evaluate whether the use of ABPM in the primary care setting would improve clinical outcomes.

In conclusion, BP measurements performed by physicians in primary care are less accurate than 24-hour ABPM. This could lead to limited control of SAH and the loss of opportunity to optimise blood pressure measurement. Additionally, our study identified a large proportion of patients with white coat hypertension, despite the fact that the GPs were known to the patients, which suggests that ABPM may be useful as an audit tool in the primary healthcare setting. This is an important factor, considering the feasibility of the implementation of checking BP for 24 hours through ABPM in primary healthcare, as well as additional information related to the evaluation of the antihypertensive effect of the treatment used.[9] There are few studies that aim to evaluate public health programmes for BP control; this study incorporated health technology to evaluate the accuracy of SAH diagnosis by primary care physicians. Thus, along with greater attention to medical training and the implementation of SAH guidelines, this study supports recommendations regarding the utilisation of 24-hour ABPM, aiming at improving the efficacy of the treatment of hypertension in the primary healthcare environment.

Acknowledgement

We thank Andy Haines of the London School of Hygiene and Tropical Medicine for his helpful comments.

References

1. Schillaci G, Pucci G. Central and 24-h blood pressure: dwarfs standing upon the shoulders of giants? *J Hypertens* 2011;**29**:430-3.
2. Kearney PM, Whelton M, Reynolds K *et al*. Worldwide prevalence of hypertension: a systematic review. *J Hypertens* 2004;**22**:11-19.
3. Amar J. Patients with resistant hypertension. *J Hypertens* 2007;**25**(Suppl1):S3-S6.
4. de la Sierra A. Blood pressure control in the hypertensive population. What else the doctor can do? *J Hypertens* 2010;**28**:1129-30.
5. Lim SS, Vos T, Flaxman AD *et al.* A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;**380**:2224-60.
6. Gus I, Harzheim E, Zaslavsky C *et al.* Prevalence, awareness, and control of systemic arterial hypertension in the state of Rio Grande do Sul. *Arq Bras Cardiol* 2004;**83**:424-428;429-33.
7. Zaninelli A, Parati G, Cricelli C *et al.* Office and 24-h ambulatory blood pressure control by treatment in general practice: the 'Monitoraggio della pressione ARteriosa nella medicina TErritoriale' study. *J Hypertens* 2010;**28**:910-17.
8. http://apps.who.int/iris/bitstream/10665/79059/1/WHO_DCO_WHD_2013.2_eng.pdf. Acesso em 29/04/2013.
9. Rodriguez-Roca GC, Alonso-Moreno FJ, Garcia-Jimenez A *et al.* Cost-effectiveness of ambulatory blood pressure monitoring in the follow-up of hypertension. *Blood Press* 2006;**15**:27-36.
10. Bobrie G, Clerson P, Ménard J *et al.* Masked hypertension: a systematic review. *J Hypertens* 2008;**26**:1715-25.
11. Hansen TW, Jeppesen J, Rasmussen S *et al.* Ambulatory blood pressure and mortality: a population-based study. *Hypertension* 2005;**45**:499-504.
12. Redon J, Lurbe E. Nocturnal blood pressure versus non dipping pattern: what do they mean? *Hypertension* 2008;**51**:41-2.
14. Hansen TW, Li Y, Boggia J *et al.* Predictive role of the nighttime blood pressure. *Hypertension* 2011;**57**:3-10.
13. Nobre F, Coelho EB. [3 decades of AMBP–24-hour ambulatory monitoring of blood pressure. Paradigm changes in the diagnosis and treatment of arterial hypertension]. *Arq Bras Cardiol* 2003;**81**:428-34.
15. Mancia G, Sega R, Bravi C *et al.* Ambulatory blood pressure normality: results from the PAMELA study. *J Hypertens* 1995;**13**:1377-90.
16. Burnier M, Grassi G. Ambulatory blood pressure monitoring in diabetic patients: new data, new questions. *J Hypertens* 2011;**29**:198-200.
17. Parati G, Ibsen H. Twenty-four-hour ambulatory blood pressure profiles of high-risk patients in general practice: data from an ambulatory blood pressure monitoring registry. *J Hypertens* 2007;**25**:929-33.
18. Gorostidi M, Sobrino J, Segura J *et al.* Ambulatory blood pressure monitoring in hypertensive patients with high cardiovascular risk: a cross-sectional analysis of a 20,000-patient database in Spain. *J Hypertens* 2007; **25**:977-84.
19. Zanchetti A, Bond MG, Hennig M *et al.* Calcium antagonist lacidipine slows down progression of asymptomatic carotid atherosclerosis: principal results of the European Lacidipine Study on Atherosclerosis (ELSA), a randomized, double-blind, long-term trial. *Circulation* 2002;**106**:2422-7.
20. Ohkubo T, Imai Y. Predicting cardiovascular risk using ambulatory blood pressure. *JAMA* 2000;**283**:475; author reply 476.
21. Burr ML, Dolan E, O'Brien EW *et al.* The value of ambulatory blood pressure in older adults: the Dublin outcome study. *Age Ageing* 2008; **37**:201-06.
22. Dolan E, Stanton A, Thijs L *et al.* Superiority of ambulatory over clinic blood pressure measurement in predicting mortality: the Dublin outcome study. *Hypertension* 2005;**46**:156-61.
23. Little P, Barnett J, Barnsley L *et al.* Comparison of agreement between different measures of blood pressure in primary care and daytime ambulatory blood pressure. *BMJ* 2002; **325**:254.
24. Vaz-de-Melo RO, Toledo JC, Loureiro AA *et al.* [Absence of nocturnal dipping is associated with stroke and myocardium infarction]. *Arq Bras Cardiol* 2010;**94**:79-85.
25. Kaya MG, Yarlioglues M, Gunebakmaz O *et al.* Platelet activation and inflammatory response in patients with non-dipper hypertension. *Atherosclerosis* 2010;**209**:278-82.
26. Metoki H, Ohkubo T, Kikuya M *et al.* Prognostic significance for stroke of a morning pressor surge and a nocturnal blood pressure decline: the Ohasama study. *Hypertension* 2006;**47**:149-54.
27. O'Brien E. Ambulatory blood pressure measurement: the case for implementation in primary care. *Hypertension* 2008;**51**:1435-41.
28. Pickering TG. Should white coat hypertension be treated? *J Clin Hypertens* 2005;**7**:550-3.