Successive blood pressure measurements to evaluate suspected and treated hypertension

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Introduction **According to the published literature, blood pressure (BP) measurements performed in the outpatient clinical setting are often inaccurate. The white coat effect and improper technique are the main causes of this imprecision. Construction of a set of readings without them could improve the accuracy of BP measurement.**

Objective **To evaluate the accuracy and agreement of successive office BP measurements using the awake blood pressure average (ABPa) as the gold standard.**

Methods **BP was measured in 852 patients using three techniques: in office (OBPa); seven successive measurements performed by a nurse using an automatic device; and 24 h of ambulatory BP monitoring. BP averages (BPa) were obtained from the nurse's measurements: 1–2BPa (first and second), 3–7BPa (third to seventh), and 1–7BPa (first to seventh). OBPa and successive measurements were tested against ABPa by calculating the following: average difference in BP of 1–2BPa, 3–7BPa and OBPa, and the area under the curve.**

Results **Among the 834 patients eligible, 374 (43.9%) were considered to be hypertensive on the basis of the ABPa (≥135/85 mmHg). 3–7BPa showed the lowest average difference (4/3 mmHg). By contrast, OBPa showed the highest result (21/11 mmHg). The mean difference with 1–2BPa was 8/4 mmHg. The areas under the curve were better with 3–7BPa (0.82–0.85) and 1–2BPa (0.82–0.83) than OBPa (0.67–0.71) for both systolic and diastolic BP.**

Conclusion **All means from successive measurements showed a better precision than OBPa, even the two first readings. However, more research needs to be carried out before recommendation of the use of this technique in routine practice.** ***Blood Press Monit*** **21:69–74**

Blood Pressure Monitoring 2016, **21**:69–74

Keywords: blood pressure ambulatory monitoring, blood pressure determination, diagnosis, hypertension

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Received 12 March 2015 **Revised** 1 September 2015
Accepted 3 September 2015

Introduction

Over the last decade, some evidence has emerged on the imprecision of clinical blood pressure (BP) measurements [1,2]. At the same time, there is substantial evidence showing many advantages of ambulatory blood pressure monitoring (ABPM) beyond office BP measurement, for example, a large number of BP readings, a superior prognostic value, absence of observer bias, digit preference, and 'white coat' effect (WCE), among many others [3,4]. However, there is no consensus in the scientific community on whether ABPM is ready to replace clinic BP [5,6]. Few studies have shown that it is possible to predict the daytime average utilizing the mean of five sequential BP office readings using a fully automated device [7]. Thus, successive measurements could become a good choice to achieve a precision of BP values in the clinical setting. Thus, we need to know more about the impact of reading numbers on the accuracy of office BP.

All hypertension guidelines include BP values as the basis of the most important clinical decisions for the management of hypertension [8,9]. Also, the guidelines emphasize that to obtain accurate values, a standardized and well-performed BP measurement is necessary [10].

The unreliability of clinical BP measurement is frequently associated with the WCE [11]. Physicians frequently fail to perform accurate BP measurements [12], which can be explained by the rounding of values and a limited number of BP readings. The WCE and improper technique, mostly rounding and a limited number of readings, are the primary sources of error in clinical BP measurements [13].

Inaccurate BP assessment is a common and relevant issue in healthcare and leads to overdiagnosis of hypertension status [14], incorrect treatment decisions [15], and overtreatment, resulting in additional costs because of the unnecessary prescription of antihypertensive drugs [16].

In 2011, the National Institute for Health and Clinical Excellence recommended the routine use of ABPM for the initial diagnosis of hypertension as a solution for the inaccuracy of office BPs [17]. This decision was based on the many advantages of the use of ABPM over office BP, and also on the basis of a cost-effectiveness analysis, which showed that ABPM minimizes costs by avoiding the prescription of

DOI: 10.1097/MBP.0000000000000161

unnecessary antihypertensive drugs [18]. Nevertheless, some specialists still question whether this decision is suitable for all countries because the implementation of this recommendation is somewhat challenging [6,19].

Surveys have shown that it is possible to achieve more accurate BP values by restructuring clinical BP measurements. First, BP values from nonphysician readings are lower than readings by doctors [20]. Second, to significantly reduce the variance in BP values within patients and to properly classify patients as normotensive or hypertensive, health professionals should perform five to seven readings per visit [21]. Also, BP-measuring devices allow the measurement of BP without rounding and are not associated with the WCE [22–24].

Therefore, on the basis of all of the above evidence, we hypothesized that a new approach, without the limitations of office BP, should result in more precise results than the more typical BP measurement methods. Therefore, we aimed to evaluate the accuracy of successive office BP measurements using the awake ambulatory blood pressure average (ABPa) as the gold standard. Consequently, we designed a configuration of office BP measurements comprised of seven sequential readings performed by a nurse using an automatic BP-measuring device.

Methods

Participants and location

Between January and September 2013, all patients older than 18 years of age who were scheduled to create an ABPM record in a cardiology clinic in Uberaba – Brazil were considered for enrollment. Each patient was referred from 57 doctors' offices, 52 outside and five inside the clinic, because of recently diagnosed high BP or uncontrolled treated hypertension. In the doctors' offices, all patients made a medical appointment and had their BP measured by physicians.

Exclusion criteria

Patients who did not fulfill all of the following criteria were excluded: 24-h recording with at least 70% of expected measurements, 20 valid awake measurements, and seven valid asleep measurements (time reported by patients) [25].

Data collection

On the day scheduled for ABPM, they were requested to take part in the study. After obtaining informed consent, a nurse measured the weight, height, and waist circumference of the patients. Also, personal data and history of current and past elevated BP, medication, personal risk factors, and previous personal and familial cardiovascular disease were also collected. Thus, without any resting period, the nurse carried out seven sequential BP measurements every 2 min using an appropriate cuff, taken from the patient's nondominant arm placed at the heart level, with the patient sitting on a chair and not preceded by 5 min of a quiet resting period [10]. The seven measurements were performed in a doctor's office inside the clinic. A Microlife-BP3BTOA (Onbo Eletronic Co., Shenzhen, China) automatic device was used. Moreover, three averages from the seven readings were obtained for comparison with ABPa: 1–2BPa (BP1 and BP2), 3–7BPa (BP3 to BP7), and 1–7BPa (BP1 to BP7). Next, every patient underwent at least 24 h of ABPM using a standardized cuff on the nondominant arm and a Mobil-Graph-NG device (Cardios, São Paulo, Brazil). Both electronic devices have been validated previously for accuracy [26, 27]. All patients answered a questionnaire on any undesired reactions during ABPM. The data collected by the nurse and the ambulatory BP measurements were always obtained in the morning between 7:30 a.m. and 11:30 am. Furthermore, every reading performed by the doctors on the day that the patients were referred for ABPM was located and recorded. On the basis of these registers, the office BP average (OBPa) was calculated for each patient. Fifty-seven doctors performed 846 readings, approximately one for each patient. Finally, the cardiovascular risk was computed using the collected data and 1–2BPa [28].

Data analysis

The ABPM measurements were analyzed using the DynaMAPA – Cardios software (Cardios) after checking their quality on the basis of the guidelines for BP monitoring [25] published by the European Society of Hypertension. Study data were analyzed using the Epi Info 3.5.2 (Centers for Disease Control and Prevention, Atlanta, Georgia, USA) and MedCalc 12.7.3.0 (MedCalc Software, Ostend, Belgium) software programs.

The following typical statistics were used to evaluate the results: mean, lowest value, highest value, SD, confidence interval, and proportion. Patients were classified as having hypertension on the basis of a cut-off value of ABPa of at least 135/85 mmHg [25]. Thus, for the tested BP measurements, the area under the curve (AUC) was calculated using a cut-off value of at least 140/90 mmHg for hypertension [9]. Repeated measurement analysis and Tukey's honest significant difference test were used for retrospective comparisons to estimate whether the mean values were significantly different. Also, the concordance correlation coefficient (P_C) was calculated to evaluate the agreement and accuracy between the pressure values of all tested BP and ABPa. The Bland–Altman test was carried out to better assess the agreement of OBPa and 3–7BPa with ABPa. Finally, the proportion of values of OBPa ending in a zero was determined. The sample size was calculated on the basis of 640 patients with a degree of discordance in diagnostic performance between measurements of 2% or more, a power of 95%, and an α value of less than 0.05. Within the same sample size, it is possible to consider a difference in the mean BP of 2 mmHg, with an SD of 10 or more.

The study and consent procedures were approved by the Ethics Committees at Sirio-Libanês Hospital – São Paulo – Brazil (SLH 2013-02). Every participant signed an informed consent form.

Results

In this study, 852 patients were recruited. Data from 834 patients were analyzed after the exclusion of 18 patients because of fulfillment of one or more exclusion criteria. Table 1 summarizes the demographics and clinical characteristics of the sample. There was a high predominance of white patients (65.6%), patients with self-characterized hypertension (48.1%), obese patients (40.1%), and individuals with a high waist circumference (50.1%). Slightly more than one-half (52.3%) of the patients were categorized as having moderate, high, or very high cardiovascular risk.

Table 2 lists the systolic and diastolic BP means of ABPa, all means-tested, and the average of the first (1-BPa) and seventh (7-BPa) measurements by the nurse. The average difference between BP values from OBPa to 1-BPa and 1-BPa to 7-BPa was 12/7 and 6/1 mmHg, respectively. An analysis of variance using Tukey's test showed that both systolic and diastolic ABPa differed significantly from all tested means ($P < 0.001$). Nevertheless, measurement comparisons showed no significant differences between the systolic BP of 3–7BPa and 1–7BPa ($P = 0.14$) or between the diastolic BP of 1–2BPa, 3–7BPa, and 1–7BPa ($P > 0.09$). In all other comparisons, significant differences were found.

Among the 834 patients assessed, 374 (43.9%) were considered to be hypertensive on the basis of the ABPa (≥135/85 mmHg). Figure 1 shows the outcomes of the area under the receiver operating characteristic curve. Both in the systolic and in diastolic BP, we noted that all averages from successive measurements achieved much higher outcomes for AUC than OBPa. However, there was no significant difference in AUC results among 1–2BPa, 3–7BPa, and 1–7BPa.

In Table 3, the results of the concordance correlation coefficient (P_C) are presented. The strength of agreement of OBPa P_C values was considered relatively poor, although the other values were quite good for comparative BP data.

Table 1 Demographics and clinical characteristics of the sample

Variables	Results
Age (years) [mean ± SD (range)]	48.3 ± 14.6 (18–90)
Sex – women [*n* (%)]	422 (50.6)
Ethnicity – white [*n* (%)]	547 (65.6)
Hypertension [*n* (%)]	406 (48.7)
Antihypertensives drug use [*n* (%)]	388 (46.5)
Number of antihypertensive[a] [mean ± DP (range)]	1.6 ± 0.9 (0–5)
Diabetes [*n* (%)]	77 (9.2)
Use of statins [*n* (%)]	151 (18.1)
Active smoking [*n* (%)]	77 (9.2)
BMI (kg/m^2) [mean ± DP (range)]	29.1 ± 4.1 (17.5–45.9)
Waist circumference risk [*n* (%)]	418 (50.1)
Obesity [*n* (%)]	334 (40.1)
Cardiovascular risk[b] [*n* (%)]	
Average risk	88 (10.6)
Low risk	309 (37.1)
Moderate risk	276 (33.1)
High risk	91 (10.8)
Very high risk	70 (8.4)

[a]Values are absolute numbers (*n*), proportions (%), mean ± SD, range (minimum–maximum). BMI, obesity BMI ≥ 30 kg/m^2; at risk waist circumference > 88 cm (women), > 102 (men).
[b]Stratification of cardiovascular risk according to the 2007 Guidelines for the Management of Arterial Hypertension.

Table 2 Mean tested and standard blood pressures (mmHg)

	Mean systolic BP ± SD	Mean diastolic BP ± SD
OBPa	149 ± 19.4	92 ± 11.7
1–2BPa	136 ± 17.3	85 ± 11.2
3–7BPa	132 ± 15.0	84 ± 11.1
1–7BPa	133 ± 16.0	84 ± 11.0
ABPa	128 ± 12.8	81 ± 11.3
1-BPa	137 ± 18.2	85 ± 11.6
7-BPa	131 ± 17.0	84 ± 11.8

BP values are mean ± SD.
1–2BPa, BP1 and BP2 average; 1–7BPa, BP1 to BP7 average; 1-BPa, average from the first reading made by a nurse; 3–7BPa, BP3 to BP7 average; 7-BPa, average from the seventh reading made by a nurse.
ABPa, awake ambulatory blood pressure; BPa, blood pressure average; OBPa, doctors BP readings average BP.
$P < 0.0001$ for comparisons between all tested BP averages and awake BP average.
$P = 0.14$ for comparisons between systolic BP of 3–7BPa and 1–7BPa.
$P > 0.09$ for comparisons between diastolic BP of 1–2BPa, 3–7BPa, and 1–7BPa.

Figure 2 shows the Bland–Altman plots of the differences in BP between 3–7BPa and ABPa as well as between OBPa and ABPa. The agreement is summarized on the basis of the mean difference. The average difference compared with ABPa was significantly lower with 3–7BPa (4/3 mmHg) than OBPa (21/11 mmHg). In addition, a smaller dispersion of values in 3–7BPa compared with OBPa indicated a better agreement with awake BP.

The proportion of systolic and diastolic readings ending in zero for doctors' readings (OBPa) was calculated to be 68.0 and 69.5%, respectively.

Adverse ABPM events

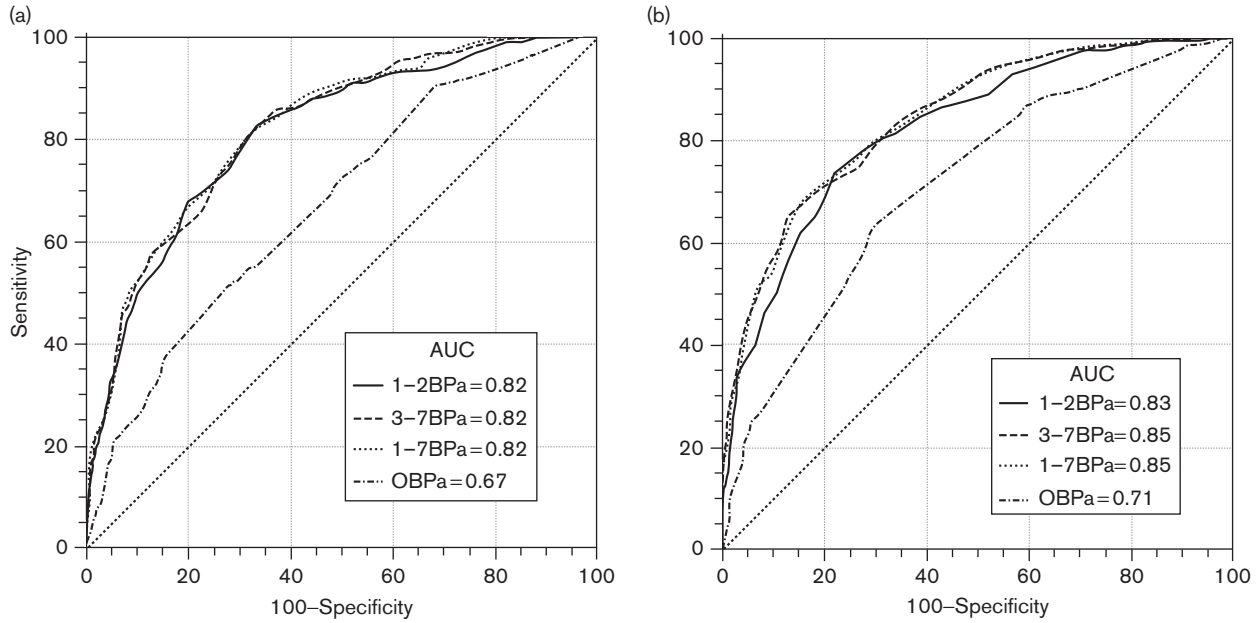
One hundred and four patients (12.5%) reported 126 undesired reactions; sleep disturbances (72 events) were the most common. However, patients reported other adverse reactions, pain or local discomfort (33 events), swelling (14 events), topical reactions (five events), hematoma, or bruising (two events). The intensity was reported as mild for 65 patients, moderate in 37 patients, and severe for two patients.

Discussion

Clinical BP measurement has shown low accuracy for the diagnosis of hypertension and evaluation of hypertension control [1,2]. The main reason for this imprecision is the WCE and poor or inconsistent measurement techniques [12,13].

This study shows that successive measurements taken by a nurse in an office setting can improve the accuracy of clinical BP, making these measurements more precise and reliable. OBPa showed the highest difference in the mean BP during the daytime (21/11 mmHg), whereas 3–7BPa showed the lowest difference (4/3 mmHg).

Fig. 1



The area under the receiver operating characteristic (ROC) curve, systolic (a) and diastolic (b) of 1–2BPa, 3–7BPa, 1–7BPa, and OBPa. AUC, area under the curve; 1–2 BPa, BP1 and BP2 average; 3–7BPa, BP3 to BP7 average; 1–7BPa, BP1 to BP7 average; OBPa, office blood pressure average.

Table 3 Concordance correlation coefficient (P_C) (95% CI)

	1–2BPa	3–7BPa	1–7BPa	OBPa
Systolic	0.53 (0.48–0.68)	0.63 (0.59–0.67)	0.61 (0.57–0.65)	0.19 (0.16–0.22)
Diastolic	0.67 (0.63–0.70)	0.72 (0.68–0.75)	0.71 (0.68–0.74)	0.31 (0.27–0.37)

Values are concordance correlation coefficient (P_C) and 95% confidence interval (CI) to systolic and diastolic tested BP measurements.
1–2BPa, BP1 and BP2 average; 3–7BPa, BP3 to BP7 average; 1–7BPa, BP1 to BP7 average.
BPa, blood pressure average; OBPa, doctors BP readings average.

The AUC analysis was consistent with this result, showing that 1–2BPa, 3–7BPa, and 1–7BPa can better discriminate between normotensive and hypertensive patients compared with OBPa. The Bland–Altman method and concordance correlation coefficient confirmed the superiority of 3–7BPa over OBPa by showing better agreement with awake ambulatory BP.

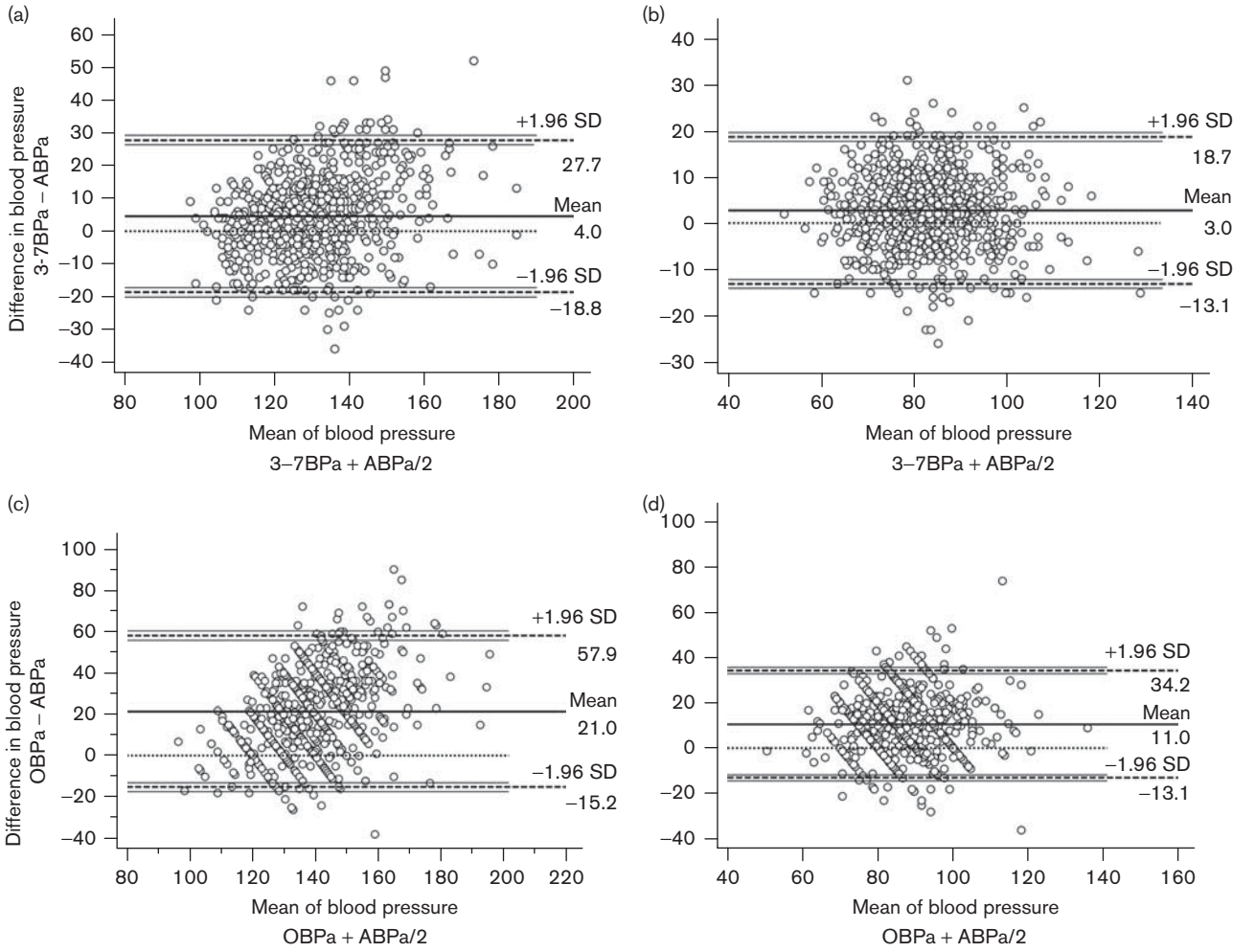
The explanation for this improved performance could be that BP values decreased significantly over the course of an office visit when the nurse performed the first BP measurement and continued to decrease with successive measurements. That is, there was a marked reduction in WCE from routine office BP to the first two BPs. The sequential measurements showed a small but significant additional decrease in systolic BP between the first and the seventh nurse measurement.

On comparing the results in Fig. 1, the AUC of 1–2BPa did not show any difference from the other nurse measurements tested. Therefore, it may be sufficient to have a nondoctor perform two measurements with an automatic device to improve the performance of office BP readings.

These results are comparable with other studies using a similar set of BP measurements and show that a different set of readings reduces the WCE to a different magnitude as well. Using the awake BP as the gold standard, Little *et al.* [20] reported a mean difference of 19.9/12.6 mmHg for routine doctors' BP (three readings). Furthermore, in the same research with a standardized set of three readings taken by doctors using a calibrated mercury sphygmomanometer, the authors found a mean difference of 18.9/11.4 mmHg. We found an average difference of 21/11 mmHg for physicians' measurements (OBPa), which is very similar to that reported by Little and colleagues.

However, some studies have reported that a similar technique of successive BP measurements using fully automatic devices (AOBP) with readings taken when the patient is alone can predict awake BP. Using a set of five such readings, Myers [24] found a mean difference against awake BP of $-2/-2$ mmHg and a correlation coefficient (r) of 0.62/0.72. Our best set of measurements (3–7BPa) showed a mean difference of 4/3 mmHg and a concordance correlation coefficient (P_C) of 0.63/0.72.

Fig. 2



The Bland–Altman plot of 3–7BPa (a, b) and OBPa (c, d) versus ABPa. 3–7BPa, BP3 to BP7 average; ABPa, awake blood pressure average; OBPa, office blood pressure average.

This could mean that a set of measurements requiring activation of the readings by a nurse shows a residual WCE and cannot predict ABPa.

One limitation of this study could be that the data were collected in a referral center and the population of the study is mostly composed of individuals with high office BP showing a referral bias. However, this could only limit generalization to an unselected patient population. Another limitation is that as the readings were taken by a nurse and lasted around 13 min, it could be that successive measurements may not be easy to carry out in routine practice. However, measurment of BP with the automatic device is very easy. Moreover, this could be done by any trained health staff, not necessarily a nurse, or even by the patient alone as shown by studies using AOBP [24]. Furthermore, analysis of the results of 1–2BPa shows that the WCE can be reduced significantly by a set of readings performed in a shorter time. Obviously, less time for measurements and cheaper trained staff could decrease the personnel costs.

The concept of AOBP is based on the elimination of human involvement in BP measurements [24], although successive measures search only the elimination of doctor involvement. As opposed to AOBP, the lack of evidence and the personnel costs restrict recommendation of successive readings for routine practice. However, taking into account the costs of BP devices used by both techniques, the low-cost successive measurements set, for example, using fewer readings and cheaper trained staff or even with the patient alone using new BP devices with memory to BP values, could help this technique to find a place in routine practice, mainly in the public health sector of low income countries.

Moreover, to determine whether successive readings can gain a place in routine practice, further research with

them or their future variations is necessary by performing validation in large primary centers, making comparisons to predict organ damage and cardiovascular risk against ABPM, and also to compare cost effectiveness with AOBP.

Finally, this study does not seek to replace ABPM or physician BP measurements, but rather, it is aimed at reconfiguring office BP measurements to obtain more precise BP values.

Conclusion

Clinical BP measurement can be restructured using a successive BP measurement technique, which is more accurate because all averages extracted from the set, even from the first two readings, can reduce the WCE significantly. However, more research is necessary before this technique can be recommended for making decisions in the treatment of high BP.

Acknowledgements

The authors thank the patients, staff, and physicians at the Cardiac Diagnostic Center. In addition, they thank all physicians from Uberaba, who allowed us to access medical record information for their patients who participated in the study. The first author thanks Gilson and Jose Mauricio, their instructors, who helped them develop the study and facilitated the experiments conducted in this project.

Conflicts of interest

There are no conflicts of interest.

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