

# Is the area under blood pressure curve the best parameter to evaluate 24-h ambulatory blood pressure monitoring data?

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**Background** Ambulatory blood pressure monitoring (ABPM) provides relevant data about blood pressure over a 24-h period. The analysis of parameters to determine the blood pressure profile from these data is of great importance.

**Objectives** To calculate areas under systolic and diastolic blood pressure curves (SBP-AUC/DBP-AUC) and compare with systolic and diastolic blood pressure load (SBPL/DBPL) and 24-h systolic and diastolic blood pressure (24-h SBP/24-h DBP) in order to determine which provides the best correlation with left ventricular mass index (LVMI).

**Methods** ABPM measurements (1143 individuals) were analyzed to obtain 24-h SBP/24-h DBP, SBPL/DBPL, and SBP-AUC/DBP-AUC, using Spacelabs (90207) and CardioSistemas devices. Left ventricular mass was determined using an echocardiograph HP Sonos 5500 and LVMI was calculated.

**Results** The correlations between all possible pairs within the group 24-h SBP/SBPL/SBP-AUC and 24-h DBP/DBPL/DBP-AUC were high and statistically significant. The correlations between 24-h SBP/24-h DBP and SBP-AUC/DBP-AUC with SBPL/DBPL close to 100%, were lower than those mentioned above. The correlations of the parameters obtained by ABPM with LVMI were also high and

statistically significant, except for blood pressure load between 90 and 100%, and for 24-h SBP of 135 mmHg or less and SBPL higher than 50%.

**Conclusions** SBPL/DBPL and SBP-AUC/DBP-AUC can be used for the evaluation of ABPM data owing to the strong correlation with 24-h SBP/24-h DBP and with LVMI, except when SBPL is close to 100% or 24-h SBP is below 135 mmHg but SBPL is above 50%. SBP-AUC/DBP-AUC, however, are a better alternative because they do not have the limitations of blood pressure load or even of 24-h blood pressure present. *Blood Press Monit* 10:263–270 © 2005 Lippincott Williams & Wilkins.

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**Keywords:** ambulatory blood pressure monitoring, area under the blood pressure curve, blood pressure load, left ventricular mass index

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## Introduction

Ambulatory blood pressure monitoring (ABPM) data allow 24-h blood pressure evaluation. The criteria more frequently used for this evaluation are 24-h systolic blood pressure (24-h SBP) and 24-h diastolic blood pressure (24-h DBP), systolic blood pressure load (SBPL), and diastolic blood pressure load (DBPL) [1].

Twenty-four-hour blood pressure is used to define normal 24-h ambulatory blood pressure (ABP) because it shows a high correlation with target-organ damage, which is better than that obtained with office blood pressure measurements [2]. Twenty-four-hour ABP, however, has been reported to have limitations when applied to patients with 'high-normal' arterial blood pressure who may show normal 24-h ABP even though their blood pressure loads (BPLs) are altered [3]. An alternative method to define 24-h ABP is BPL, defined as the percentage of systolic and diastolic measurements above a specific limit. These values are very important because of their correlation

with target-organ damage and hypertension [4,5]. Most of the main guidelines, however, do not even cite them [6–9], owing to the fact that two individuals may have the same percentage of readings above a specific limit but different 24-h blood pressure. In patients with moderately severe hypertension, for example, BPL cannot distinguish between two individuals, both with a BPL equal to 100%, but with markedly different 24-h ABP [10]. This represents a limitation of the use of this criterion for interpretation of ABPM data. As there are limitations to the use of 24-h ABP when it is below normal limits but BPL is above the normal values, consequently there are limitations for the use of both BPL and 24-h blood pressure under specific circumstances.

In fact, to overcome these limitations, it was suggested that the calculation of BPL would be improved by obtaining the area under the blood pressure curve defined by thresholds of 140/90 mmHg during the daytime and 120/80 mmHg during the night-time [11,12].

Although White *et al.* [12,13] studied the integration of the area under the blood pressure curve and obtained a significant correlation between blood pressure values and hemodynamic levels, the correlations between parameters like SBPL, DBPL, systolic blood pressure area under the curve (SBP-AUC), diastolic blood pressure area under the curve (DBP-AUC) and 24-h SBP and 24-h DBP have not been compared using the same data set at the same time. Furthermore, it is not known whether area under the blood pressure curve shows a good correlation with 24-h blood pressure and the BPL. In addition, the correlation of these three parameters with left ventricular mass index (LVMI) is unknown.

Thus, the objective of the present study was to carry out the following determinations on a large number of individuals: to calculate areas under SBP and DBP curves and compare them with systolic and diastolic blood pressure load (SBPL/DBPL) and 24-h blood pressure in order to determine which provides the best correlation with LVMI.

## Methods

The ABPM data of patients seen at the Hypertension Unit of the Medical School of Ribeirão Preto, São Paulo University, from 1996 to 1999, were included in the present study without any restriction regarding race, age, sex, blood pressure level, social level, or antihypertensive treatment. The study was conducted on 1143 study participants, 619 of whom (54.2%) were hypertensive. All hypertensive patients were on treatment and were being monitored for evaluation of blood pressure control with the treatment. In addition, 524 patients (45.8%) were being monitored for analysis of their 24-h blood pressure profile. Each patient was studied only once.

The ABPM was performed using validated automatic oscillometric devices (Spacelabs model 90207, Redmond, Washington, USA) or CardioSistemas – DinaMAPA, São Paulo, SP, Brazil) and an echocardiogram was obtained with an echocardiograph HP Sonos 5500 (Phillips, Boston, Massachusetts, USA).

Measurements were taken every 15 min during the daytime (0700 to 2300 h) and every 20 min during the night-time (2301 to 0659 h). A cuff of appropriate dimensions was wrapped around the non-dominant arm. According to the software specifications, blood pressure measurements that were considered to be inappropriate for the analysis were automatically deleted. Twenty-four-hour systolic and diastolic blood pressure and BPLs were considered for analysis. To calculate the BPL, we used the following criteria: >140/90 mmHg daytime and >120/80 mmHg night-time.

A computer program employed to calculate the area under the blood pressure curve was developed with the Visual Fox

Pro 3 software (Microsoft, Redmond, Washington, USA). The program used normal daytime and night-time SBP and DBP values, the time defining these two periods, and the blood pressure values [7]. Thus, the parameters used for analysis were time, blood pressure values, and normal limits defined for 24-h blood pressure (140/90 mmHg for the daytime and 120/80 mmHg for the night-time).

Left ventricular mass was obtained by transthoracic echocardiography, performed in an aleatory form in 329 participants, and LVMI was calculated by the Devereux formula [14]. LVMI was then correlated with the area under the blood pressure curve, BPL, and 24-h blood pressure. On this basis, the data can represent the population studied.

Data are reported as mean  $\pm$  SD. The relationship between 24-h blood pressure and age, BPL, area under the curve, and LVMI was calculated by Pearson's correlation coefficient. Twenty-four-hour blood pressure was compared according to sex using the Student's *t*-test. The association between 24-h blood pressure and BPL classification was assessed by the  $\chi^2$  test.

Areas under the curves for patients divided into subgroups according to their 24-h SBP/24-h DBP were compared with SBPL/DBPL. The level of significance was set at  $P < 0.05$  in all analyses.

The study was approved by the Research Ethics Committee of the University Hospital, Medical School of Ribeirão Preto, University of São Paulo.

## Results

SBPL/DBPL, 24-h SBP/24-h DBP, and SBP-AUC/DBP-AUC values as a function of sex are reported in Table 1. In all cases, females had lower values than males.

### Blood pressure loads and areas under the curves

Correlation of SBPL with its respective SBP-AUC was  $r = 0.85$  ( $P < 0.0001$ ) for the 0–100% interval and  $r = 0.35$  ( $P < 0.0001$ ) for the 90–100% interval. The correlations between DBPL and its corresponding DBP-AUC were  $r = 0.87$  ( $P < 0.0001$ ) and  $r = 0.27$  ( $P < 0.0448$ ) for the same intervals, respectively (Fig. 1).

### Blood pressure load and 24-h blood pressure

When correlations were established between SBPL and 24-h SBP for load variation intervals from 0 to 100% and 90 to 100%, the correlation coefficients were 0.90 ( $P < 0.0001$ ) and 0.48 ( $P < 0.0001$ ), respectively, and the correlation coefficients between DBPL and 24-h DBP for the same intervals were 0.90 ( $P < 0.0001$ ) and 0.55 ( $P < 0.0001$ ), respectively (Fig. 2).

### Areas under the curves and 24-h blood pressure

The correlation coefficient between 24-h SBP and the corresponding SBP-AUC was  $r = 0.84$  ( $P < 0.0001$ )

and the correlation coefficient between 24-h DBP and the corresponding DBP-AUC was  $r = 0.84$  ( $P < 0.0001$ ) (Fig. 3).

**Table 1 Patient's sex and distribution of systolic blood pressure loads/diastolic blood pressure loads, 24-h systolic blood pressure/diastolic blood pressure, systolic blood pressure-area under curve/diastolic blood pressure-area under curve between sexes (Student's *t*-test)**

	<i>n</i>	Mean ± SD	( <i>P</i> )
Mean age (years)	F	53.63 ± 14.88	–
	M	49.79 ± 15.48	0.0001
Male		54.2%	
Female		45.8%	
SBPL (%)	F	46.25 ± 30.74	0.0003
	M	52.79 ± 29.45	
DBPL (%)	F	30.90 ± 28.58	0.0001
	M	42.14 ± 28.54	
24-h SBP (mmHg)	F	132.60 ± 17.43	0.0453
	M	134.55 ± 15.16	
24-h DBP (mmHg)	F	79.48 ± 11.73	0.0001
	M	83.38 ± 10.47	
SBP-AUC (mmHg × h)	F	21 439.83 ± 18 436.87	0.0082
	M	24 302.45 ± 17 507.07	
DBP-AUC (mmHg × h)	F	8084.35 ± 9561.47	0.0001
	M	10 970.84 ± 9604.46	

F, female; M, male; SBPL, systolic blood pressure load; DBPL, diastolic blood pressure load; SBP, systolic blood pressure; DBP, diastolic blood pressure; SBP-AUC, systolic blood pressure area under curve; DBP-AUC, diastolic blood pressure area under curve.

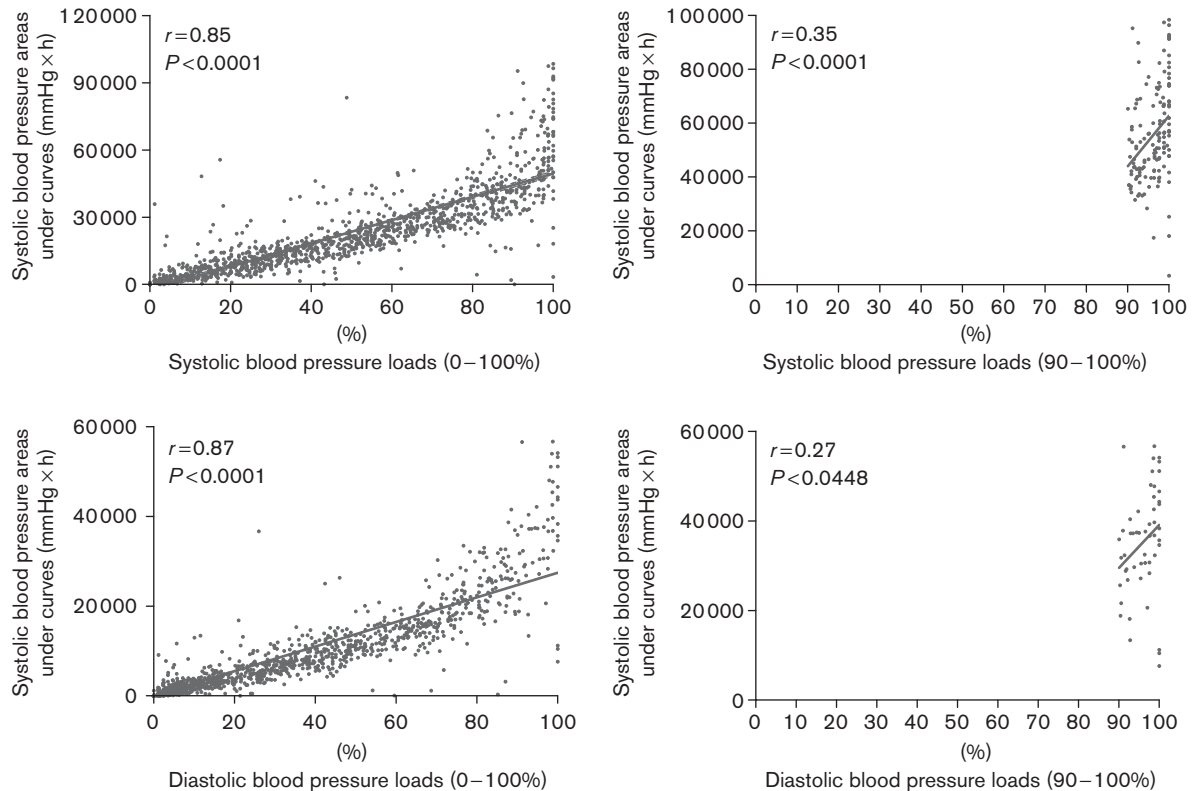
**Comparison with ambulatory blood pressure monitoring normality criteria**

The values obtained for the correlation of SBP-AUC and DBP-AUC with 24-h blood pressure were compared according to the criteria defined by the Canadian Hypertension Society Guidelines for Ambulatory Blood Pressure Monitoring [7]. These guidelines consider ABPM values to be normal when 24-h systolic/diastolic blood pressure is ≤ 130/80 mmHg, borderline when > 130 ≤ 135/> 80 ≤ 85 mmHg, and abnormal when > 135/> 85 mmHg.

In 497 (46.7%) of the total individuals assessed, 24-h SBP values were lower than 130 mmHg; in 180 (12.6%), the values ranged from 130 to 135 mmHg, and in 466 (40.7%), the values were higher than 135 mmHg. For individuals whose 24-h SBP was lower than 130 mmHg, the mean SBP-AUC was 8737.28 ± 7046.22 mmHg × h, whereas for values ranging from 130 to 135 mmHg, the corresponding SBP-AUC was 19654.03 ± 5472.18 mmHg × h. Finally, for individuals whose 24-h SBP was over 135 mmHg, the SBP-AUC was 38922.93 ± 16283.17 mmHg × h (Fig. 4).

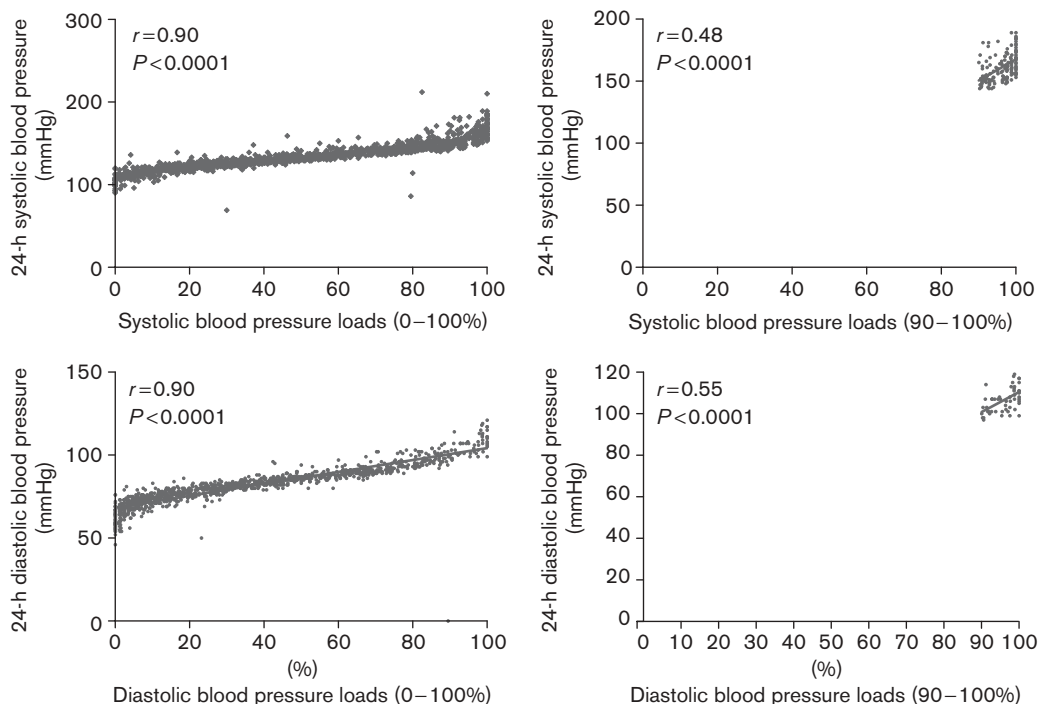
With regard to 24-h DBP, absolute and percentage distributions were from 506 individuals (49.3%) for values

**Fig. 1**



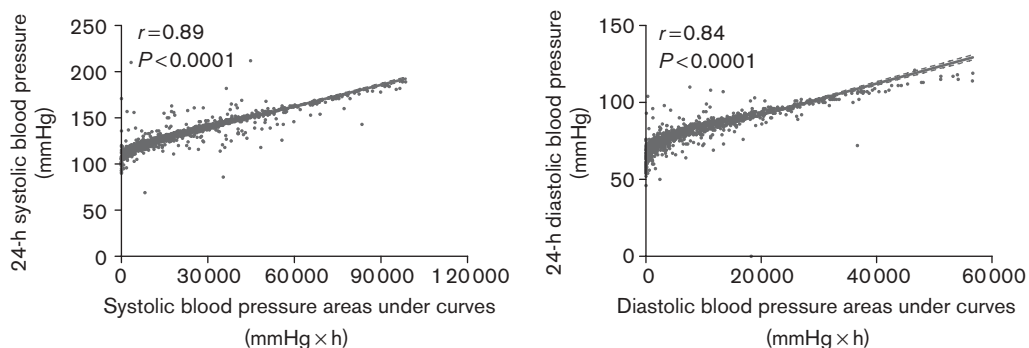
Correlations between systolic blood pressure areas under curves and diastolic blood pressure areas under curves with systolic blood pressure loads and diastolic blood pressure loads from 0 to 100% and from 90 to 100%.

Fig. 2



Correlations between 24-h systolic blood pressure/diastolic blood pressure with systolic blood pressure loads/diastolic blood pressure loads from 0 to 100% and from 90 to 100%.

Fig. 3



Correlations between 24-h systolic blood pressure and diastolic blood pressure with systolic blood pressure areas under curves and diastolic blood pressure areas under curves.

up to 80 mmHg, 255 (15.4%) for values from 80 to 85 mmHg, and 382 (35.3%) for values higher than 85 mmHg. The respective DBP-AUC for these groups were  $2484.24 \pm 2819.15$ ,  $7793.54 \pm 2878.70$ , and  $19586.86 \pm 9788.47$  mmHg  $\times$  h (Fig. 4).

The correlations between the various parameters and LVMI ( $n = 329$ ) were 0.54 ( $P < 0.0001$ ) for SBP-AUC,

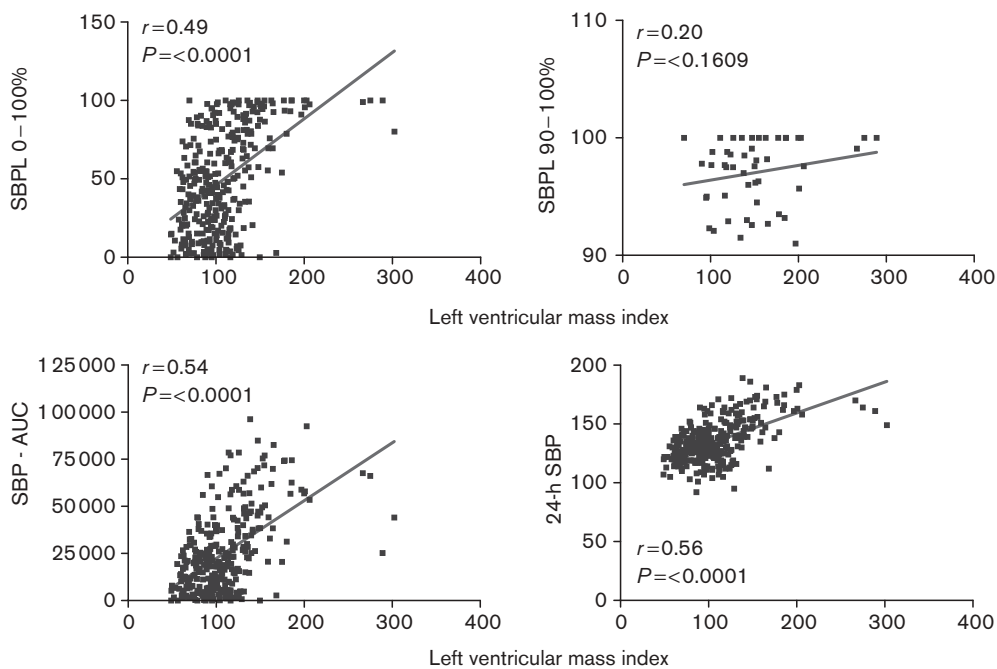
0.29 ( $P < 0.0001$ ) for DBP-AUC, 0.56 ( $P < 0.0001$ ) for 24-h SBP, 0.35 ( $P < 0.0001$ ) for 24-h DBP, 0.49 ( $P < 0.0001$ ) for SBPL from 0 to 100%, 0.20 ( $P = 0.167$ ) for SBPL from 90 to 100%, 0.33 ( $P < 0.0001$ ) for DBPL from 0 to 100%, and 0.39 ( $P = 0.267$ ) for DBPL from 90 to 100%. For patients with 24-h SBP of 135 mmHg or less, but with SBPL higher than 50%, the correlation was 0.04 ( $P = 0.86$ ). We can see some of these data in Fig. 5.

Fig. 4



Mean values of area under systolic blood pressure curve for 24-h systolic blood pressure lower than 130 mmHg, from 130 to 135 mmHg and over 135 mmHg, and area under diastolic blood pressure curve for 24-h diastolic blood pressure lower than 80 mmHg, from 80 to 85 mmHg and over 85 mmHg.

Fig. 5



Correlations of systolic blood pressure load from 0 to 100% and 90 to 100% with left ventricular mass index and systolic blood pressure area under curves and 24-h systolic blood pressure with left ventricular mass index. SBPL, systolic blood pressure load; SBP-AUC, systolic blood pressure area under curve; 24-h SBP, 24-h systolic blood pressure.

**Discussion**

Twenty-four-hour blood pressure recordings contain a large amount of data that must be processed before they

can be interpreted. Several functions such as SBPL/DBPL and 24-h SBP/24-h DBP have been introduced to provide a basis to facilitate interpretation. Correlations of

these parameters with LVMI provide information about prognosis.

In the present study, we have used data from 1143 24-h ABPM records to test correlations between these parameters and LVMI, and a new criterion for ABPM evaluation (i.e. SBP-AUC/DBP-AUC).

The main result of the present study was that the correlations between all possible pairs within the group 24-h SBP/SBPL/SBP-AUC and 24-h DBP/DBPL/DBP-AUC were high and statistically significant. The correlations of 24-h SBP/24-h DBP and SBP-AUC/DBP-AUC, with SBPL/DBPL close to 100%, however, were lower than those mentioned above. The correlations of the parameters obtained by ABPM with LVMI were also high and statistically significant, except for BPL between 90 and 100%, and for 24-h SBP of 135 mmHg or less and SBPL higher than 50%.

In fact, SBP-AUC/DBP-AUC are better criteria because they do not have the limitations of BPL or even of 24-h SBP and present a better correlation with 24-h SBP/DBP and SBPL/DBPL.

BPL was defined as the percentage of blood pressure measurements higher than reference values [4] and later White and Morganroth [15] concluded that BPL correlated better with left ventricular shortening mass and peak ratio than casual blood pressure measurements. White *et al.* [10] established a correlation between left ventricular mass, its functional aspects and BPL. In this study, a limitation to the correlation was observed when BPL was close to 100%. Zachariah and Summer [16] also discussed the use of BPL for the determination of hypertension and suggested that BPL can provide unique information concerning blood pressure behavior primarily in patients with mild to moderate hypertension, for whom 24-h ABPM data may be evaluated inaccurately because of the high variability of these values. Twenty-four-hour blood pressure can be normal even when BPL has already increased. Ohkubo *et al.* [17] reported a good correlation between blood pressure values obtained by ABPM and prognosis.

In our study, only 8.5% ( $n = 97$ ) of the patients had SBP of 135 mmHg or less, but SBPL of 50% or more, whereas only 1.6% ( $n = 19$ ) had 24-h DBP of 85 mmHg or less, but DBPL of 50% or more. Other investigators [18–20] studied the use of BPL in hypertensive patients but this criterion is really limited for upper BPL values (i.e. values close to 100%). In the present investigation, only 2.7% ( $n = 31$ ) of the patients had an SBPL of 100% and 1.0% ( $n = 12$ ) had a DBPL of 100%.

White *et al.* [12], using the integration of area under the curve for 24h, reported that this parameter was signifi-

cantly correlated with blood pressure values obtained by ABPM and hemodynamic data such as cardiac output, cardiac index, and total peripheral vascular resistance. They concluded that BPL is an effective parameter to evaluate the 24-h blood pressure profile. On the basis of these findings, they also concluded that, in contrast to blood pressure, the area under the blood pressure curve had no limitations for upper values. No studies, before the present study, however, have compared area under the blood pressure curve, 24-h blood pressure, and BPL.

BPL has been used to determine the therapeutic efficacy of antihypertensive drugs. More appropriate blood pressure control was also obtained when DBPL rather than casual blood pressure measurements was used to evaluate the blood pressure profile. Zachariah *et al.* [21] studied the relationship between BPL and age and 24-h blood pressure in normotensive participants and concluded that 'men showed systolic blood pressure load higher than women over 24 hours and that both increased with age for both genders.'

In the present study, there were a higher percentage of women, which can be explained by the fact that women seek health services more frequently than men in Brazil. As also observed in the PAMELA study [22], 24-h blood pressure was significantly higher in men than in women. In contrast to the data reported by Zachariah *et al.* [21], the PAMELA study reported, however, that DBPL was higher in men than in women.

Reservations about ABPM data have been raised concerning BPL, especially for patients with severe hypertension. Nevertheless, several investigators have been using this parameter in situations such as pregnancy and others [18–20]. Mulé *et al.* [23] also concluded that for patients with mild to moderate hypertension, SBPL can be associated with adverse cardiovascular profiles.

In this investigation, areas under the blood pressure curves correlated with previously defined criteria were used for the analysis of data obtained by ABPM. Therefore, when considering 24-h systolic and diastolic blood pressure as independent variables, statistically significant correlations between SBPL and SBP-AUC and also between DBPL and DBP-AUC were demonstrated. Given the limitations suggested for BPL close to 100%, an analysis of this situation was carried out. All the correlations were statistically significant, but a stronger correlation was observed between SBPL/DBPL from 0 to 100% and SBP-AUC/DBP-AUC ( $r = 0.85$   $P < 0.0001$  for SBPL and  $r = 0.87$   $P < 0.001$  for DBPL) than for BPL ranging from 90 to 100%. For these values, which represent the upper values, the correlations with SBPL and DBPL were  $r = 0.35$  ( $P < 0.001$ ) and  $r = 0.27$  ( $P < 0.044$ ),

respectively. The same was observed when BPL and 24-h blood pressure were compared. In these cases, the correlations of systolic and diastolic blood pressure were  $r = 0.90$  ( $P < 0.0001$ ) for the interval from 0 to 100% and  $r = 0.48$  ( $P < 0.0001$ ) for the interval from 90 to 100%.

As it has been suggested that 24-h SBP may have limitations when its values are below 135 mmHg but SBPL values are higher than 50%, we focused on patients with this characteristic too. ( $n = 97$ ).

The present data indicate that the three variables (24-h blood pressure, BPL and area under the blood pressure curve) can reflect the behavior of blood pressure obtained by ABPM. Limitations exist for the use of BPL and 24-h blood pressure, but not for area under the blood pressure curve.

Thus, the area under the blood pressure curve can play an important, useful and complementary role in the evaluation of 24-h ABPM, without limitations for BPL [10] or for 24-h blood pressure [16]. The area under the blood pressure curve can be a useful criterion for the analysis of blood pressure obtained by ABPM.

LVMI was correlated with each of the parameters obtained by ABPM (24-h blood pressure, BPL and area under the blood pressure curve) in 329 patients for whom an echocardiogram was available. Good correlations were found between the parameters obtained by ABPM and LVMI, except for BPL between 90 and 100% or when the 24-h SBP was 135 mmHg or less and the SBPL was higher than 50%.

Our finding demonstrates the limitations of BPL close to 100%, which were not observed for the area under the blood pressure curve.

Similarly, when 24-h SBP values were normal but SBPL values were close to 50%, no significant correlations with LVMI were observed. This result may indicate that this condition is also a limitation in the evaluation of ABPM.

A possibility would be to establish an area under the blood pressure curve corresponding to normal values, just as it has been defined for 24-h blood pressure.

The main result of our study was that SBPL/DBPL and SBP-AUC/DBP-AUC could equally represent normality criteria for ABPM owing to their good and statistically significant correlation with 24-h SBP/24-h DBP and LVMI, except when BPL is close to 100% or 24-h SBP is below 135 mmHg, but SBPL is 50% or more.

The use of SBP-AUC/DBP-AUC as a method to evaluate ABPM is a better alternative because it is not limited as is BPL or 24-h blood pressure. Thus, SBP-AUC/DBP-AUC may be considered to be the best alternative for the evaluation of the arterial pressure behavior obtained by ABPM.

The present study has limitations. A non-selected studied population is probably the most important of them. Considering the objective of the study – evaluation of the role of the areas under the blood pressure curve – the conclusions are applicable.

Another is the fact that some echocardiography studies were conducted on hypertensive patients on treatment and others on normotensive individuals.

For a general application of these conclusions, including normality criteria, a special investigation should be done. This is a current research line of our ambulatory blood pressure monitoring. The technology for the production of the software for calculation of the area under the blood pressure curve is very simple and the method could be easily used in all ABPM laboratories.

## References

- 1 Pieper C, Pickering TG. Methods of analysis of ambulatory blood pressure data. In: Pickering TG, editor. *Ambulatory blood pressure and blood pressure variability*. London: Science Press; 1991. pp. 16.1–16.15.
- 2 Mancia G, Zanchetti A, Agebiti-Rosei E, Benemio G, De Cesaris R, Fogari R, et al. Ambulatory blood pressure is superior to clinic blood pressure in predicting treatment-induced regression of left ventricular hypertrophy. *Circulation* 1997; **95**:1464–1470.
- 3 Zachariah PK, Sheps SG, Bailey KR, Wiltgen CM, Moore AG. Reproducibility of ambulatory blood pressure load. *J Hum Hypertens* 1990; **4**:625–631.
- 4 Zachariah P, Sheps SG, Ilstrup DM, Long CR, Bailey KR, Wiltgen CM, et al. Blood pressure load – a better determinant of hypertension. *Mayo Clin Proc* 1988; **63**:1085–1091.
- 5 Bauwens F, Duprez D, Buyzere ND, Clement DL. Blood pressure load determines left ventricular mass in essential hypertension. *Int J Cardiol* 1992; **34**:335–338.
- 6 Pickering TG, Kaplan N, Krakoff L, Prisant LM, Sheps S, Weber MA, et al. Recommendations for the use of home (self) and ambulatory blood pressure monitoring. *Am J Hypertens* 1996; **9**:1–11.
- 7 Myers MG, Haynes RB, Rabkin SW. Canadian Hypertension Society guidelines for ambulatory blood pressure monitoring. *Am J Hypertens* 1999; **12**:1149–1157.
- 8 O'Brien E, Coats A, Owens P, Petrie J, Padfield PL, Littler WA, et al. Use and interpretation of ambulatory blood pressure monitoring: recommendations of the British Hypertension Society. *BMJ* 2000; **320**:1128–1134.
- 9 O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, et al. European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. *J Hypertens* 2003; **21**:821–848.
- 10 White WB, Lund-Johansen P, Omvik P. Twenty-four-hour blood pressure load as a surrogate end-point in assessing antihypertensive therapy. *J Hypertens* 1993; **11**(Suppl 4):S75–S80.
- 11 Zachariah P, Summer WE 3rd. The clinical utility of blood pressure load in hypertension. *Am J Hypertens* 1993; **6**:194S–197S.
- 12 White WB, Lund-Johansen P, Weiss S, Omvik P, Indurkha N. The relationships between casual and ambulatory blood pressure measurements and central hemodynamics in essential human hypertension. *J Hypertens* 1994; **12**:1075–1081.

- 13 White WB, Dey HM, Schulman P. Assessment of the daily blood pressure load as a determinant of cardiac function in patients with mild-to-moderate hypertension. *Am Heart J* 1989; **118**:782-795.
- 14 Devereux RB, Alonso DR, Lutas EM, Gottlieb GJ, Campo E, Sachs I, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *Am J Cardiol* 1986; **57**:450-458.
- 15 White WB, Morganroth J. Usefulness of ambulatory monitoring of blood pressure in assessing antihypertensive therapy. *Am J Cardiol* 1989; **63**:94-98.
- 16 Zachariah P, Sumner W 3rd. The clinical utility of blood pressure load in hypertension. *Am J Hypertens* 1993; **6**:194S-197S.
- 17 Ohkubo T, Hozawa A, Nagai K, Kikuya M, Tsuji I, Ito S, et al. Prediction of stroke by ambulatory blood pressure monitoring versus screening blood pressure measurement in a general population: the Ohasama study. *J Hypertens* 2000; **18**:847-854.
- 18 White WB. Relevance of the trough-to-ratio to the 24 h blood pressure load. *Am J Hypertens* 1996; **9**(Pt 2):91S-96S.
- 19 Tsioufis C, Stefanadis C, Goumas G, Pitsavos C, Toutouzas P. Relation of ambulatory blood pressure load with left ventricular geometry in untreated patients with mild-to-moderate hypertension. *J Hum Hypertens* 1999; **13**:677-682.
- 20 Hermida RC, Ayala DE. Evaluation of the blood pressure load in the diagnosis of hypertension in pregnancy. *Hypertension* 2001; **38**(Pt 2):723-729.
- 21 Zachariah P, Sheldon S, Bailey KR, Wiltgan CM, Moors AG. Age-related characteristics of ambulatory blood pressure load and mean blood pressure in normotensive subjects. *JAMA* 1991; **265**:1414-1417.
- 22 Mancia G, Sega R, Bravi C, De Vito G, Valagressa F, Cesana G, et al. Ambulatory blood pressure normality: results from the PAMELA study. *J Hypertens* 1995; **13**:1377-1390.
- 23 Mulé G, Nardi E, Andronico G, Cottone S, Raspanti F, Piazza G, et al. Relationships between 24 h blood pressure load and target organ damage in patients with mild-to-moderate essential hypertension. *Blood Press Monit* 2001; **6**:115-123.