24-Hour Blood Pressure in Normotensive Elderly Women and Elderly Women with White-Coat Hypertension

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Abstract

Background: Changes in the behavior of the circadian rhythm can be deleterious, leading to target-organ damage, which suggests that they can have a prognostic significance and, eventually, can also demand therapeutic intervention.

Objective: To describe and compare the circadian rhythms of blood pressure (BP) in normotensive elderly women and in those with white-coat hypertension (WCH).

Methods: A cross-sectional study was carried out in sample of 36 patients, aged 60-83 years, submitted to ambulatory blood pressure monitoring (ABPM) for a period of 24 hours. Nineteen normotensive elderly women and 17 with WHC were compared regarding the nocturnal dipping and the BP variability, morning increase in systolic blood pressure (SBP), pulse pressure, post-prandial hypotension and correlation of 24-hour BP means. The statistical analysis used the Student's t test, Chi-square test, Fisher's exact test and Pearson's linear correlation.

Results: The elderly women with WCH presented higher levels of SBP than the normotensive ones, between 8 am-12 pm (133 ± 8.0 mmHg *vs* 123 ± 9.0 mmHg, respectively, $p < 0.001$). The BP variability was higher in the WCH group only during the wakefulness period (between 7 am-11 pm, $p = 0.02$). A positive correlation was observed between the BMI and the SBP means at night, only in the elderly women with WCH ($r = 0.578$; $p = 0.015$ and $r = 0.488$; $p = 0.055$, respectively).

Conclusion: The elderly women with WCH presented higher SBP and diastolic blood pressure (DBP) means during the wakefulness period. In the early hours of the morning, the elderly women with WCH presented significantly higher SBP means. (Arq Bras Cardiol 2010; 94(4):405-411)

Key words: Blood pressure monitoring, ambulatory; aged; hypertension.

Introduction

In the last two decades, in Brazil, the elderly population has grown, in proportional terms, more than any other age range and it is estimated that there are currently 17.6 million elderly individuals in the country[1].

Brazilian epidemiological studies have demonstrated that the prevalence of systemic arterial hypertension (SAH) among the elderly is quite high and it is important to search for more evidence for the diagnosis, morbidity and management of the disease. Approximately 65% of the elderly individuals are hypertensive and, among women older than 75 years, the prevalence of SAH can reach 80%[2].

The elderly are prone to considerable blood pressure (BP) variability, which can lead to different diurnal patterns. These patterns are better identified with the ambulatory blood pressure monitoring (ABPM). The practical clinical consequence of these variable patterns in the elderly individual with BP is that occasional measurements can be inaccurate and/or misleading[3].

The white coat hypertension (WCH) occurs when abnormal BP levels are recorded during a visit to the medical office (≥ 140/90 mmHg) and normal values of BP are observed at the ABPM during the wakefulness period (≤ 135/85 mmHg)[4]. It is more common among the elderly than in younger individuals and patients presenting this condition can develop sustained hypertension and need careful follow-up with BP measurements, in and out of the medical office[5]. The WCH or white coat syndrome can occur in up to 20% of hypertensive elderly patients[6]. In the study by Dolan and cols., regarding the determinants of WCH, among the 5,716 individuals studied for a period of 22 years, a higher prevalence of this condition was observed among the older adults of the female sex who were nonsmokers[7].

Studies carried out in elderly individuals have suggested that the WCH is not a benign condition, as echocardiographic studies demonstrated that these patients presented a moderate increase in the left atrium dimension and left ventricular mass, associated with a tendency toward left ventricular diastolic dysfunction[8]. Among the possible alterations, the change in the behavior of the circadian rhythm in these patients can be one

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of the components involved in the deleterious mechanisms that lead to target-organ damage. Such perspective suggests that it has an important prognostic meaning and eventually, that it can demand therapeutic intervention. Therefore, the research in this area is extremely interesting.

The physiopathology of WCH consists in hemodynamic alterations that are yet to be fully elucidated, although they have great clinical relevance. The diagnosis of WCH is based on the ABPM, an examination that provides information on the BP during the daily activities and the sleep period and a more detailed analysis of the 24-hour behavior of pressure rhythms in individuals with this condition has not been described yet[9].

The objective of this study was to describe and compare the blood pressure circadian rhythms of normotensive elderly women and women with WCH for a period of 24 hours, through the analysis of ABPM.

Methods

A cross-sectional study was carried out by consecutively selecting 19 normotensive patients and 17 patients with WCH, who underwent ABPM at the Service of Nephrology of *Hospital São Lucas* of *Pontifícia Universidade Católica do Rio Grande do Sul* and met the following criteria: 1) age ≥ 60 yrs; 2) female sex; 3) patients who were not taking any medication that could affect BP for at least 4 weeks prior to the monitoring day, such as anti-hypertensive drugs, digitalis and thyroid hormones; and 4) patients who had a diagnosis of WCH as a BP measurement at the medical office, in more than two occasions, ≥ 140/90 mmHg and ≥ 140/90 mmHg at the first ABPM measurement.

The diagnosis of WCH took into account the criterion suggested by the IV Guideline for the Use of Ambulatory Monitoring of Blood Pressure, that is, the BP measurement through the conventional techniques at the medical office or clinic, in more than two occasions, being ≥ 140/90 mmHg, with ABPM measurements ≤ 135/85 mmHg during wakefulness[4]. A previously calibrated Tycos aneroid sphygmomanometer was used for the BP measurement at the office and the pressure was recorded after at least 5 minutes of rest in the sitting position, in the supported right arm.

The patients that presented the following conditions were excluded from the study: 1) dementia or other debilitating mental illnesses; 2) alcoholism or other diseases that could affect BP, such as severe valvulopathies and renal failure; e 3) use of drugs that could alter BP.

The variables of interest analyzed were: age, body mass index (BMI), systolic blood pressure (SBP) and diastolic blood pressure (DBP) at the office, 24-hr means of SBP and DBP, nocturnal and diurnal means of SBP and DBP, pulse pressure (PP), postprandial hypotension (PPH) and morning surge.

The classification of the BP variation during the wakefulness-sleep periods followed the following criterion: blood pressure dipping during sleep (%) for systolic and diastolic pressure present (≥ 10 %), absent (≤ 0 %) and attenuated (> 0 and < 10 %)[4]. A normal BP circadian rhythm was considered when there was a decrease in SBP or DBP, between the wakefulness and the sleep period, of 10% or more. Pulse pressure was defined as SBP minus DBP[10].

Postprandial hypotension was defined as the difference between the mean SBP one hour before and two hours after lunch. The BP values during the meal were excluded to avoid the influence of posture alteration or food ingestion on BP[11]. The morning surge was defined as the difference between the mean SBP of the first two hours after waking up and the mean of the three readings taken during the night[12].

The BP was monitored throughout 24 hours using a noninvasive ambulatory oscillometric BP device (Spacelabs 90207, Spacelabs Inc., Redmond, WA, USA). Each device was programmed to automatically measure the ambulatory BP every 15 minutes during the wakefulness period (from 7 am to 11 pm) and every 30 minutes during the sleep period (from 11 pm to 7 am). The device cuff was always placed on the non-dominant arm and the accuracy of the BP readings were verified against a mercury sphygmomanometer before each assessment with the ABPM. All examinations were started in the morning, between 9 am and 12 pm.

During the ABPM period, the patients were sent home and instructed to maintain their routine activities, but to avoid strenuous physical activities that could interfere with the adequate function of the BP monitor. Each patient was also asked to maintain the arm with the cuff at rest when the BP was measured and to fill out a diary with main daily activities (for instance: mealtimes, sleep time) and possible symptoms that would occur during the monitoring time. The recordings that had a minimum duration of 24 hours, with 80 valid readings, corresponding to at least 80% of the total measurements, were considered valid for the analysis.

The body mass index was calculated based on the ratio between the body weight in kilograms and the square height in meters (kg/m^2). The normal BMI was defined as BMI values between 18.5 and 24.9; overweight was defined as values between 25-29.9 and obesity was defined as values between 30 and 34.9[13].

The study hypothesis was that circadian rhythms of BP in elderly women with WCH and normotensive elderly women would be the same. To test such hypothesis, the statistical analysis was applied to the qualitative variables, which were compared between the two groups with the Chi-square test with adjusted residuals or Fisher's exact test, when necessary, to verify the association. The quantitative variables were compared by Student's t test. Pearson's coefficient was used to verify the correlations between variables and the 24-hour BP behavior. P values < 0.05 were considered statistically significant. The statistical package SPSS for Windows, release 14.0 was used in all statistical analyses.

The study protocol was approved by the Ethics Committee in Research of the Institute of Cardiology/*Fundação Universitária de Cardiologia*.

Results

Of the 36 patients selected for the study, whose ages varied from 60 to 83 years (mean = 69 ± 7 years), 19 were normotensive and 17 presented white-coat hypertension.

All women were Caucasians. Table 1 shows the clinical characteristics of the sample.

Most of the sample (33%) was between 60 and 64 years and were overweight. Smoking and snoring were more prevalent in the WCH group.

Table 2 shows the SBP and DBP means measured by ABPM in the normotensive and WCH groups at the office, during the 24-hour period, both diurnal and nocturnal. The groups presented differences only regarding the BP at the office.

Although the 24-hour variability was higher in the WCH group in comparison to the normotensive group, a significant difference was observed between the groups only during the wakefulness period (7 am to 11 pm), being higher in the WCH group (Table 2).

The postprandial BP decreased on average 5.7 ± 10 mmHg for the normotensive and 9.4 ± 15 mmHg in the WCH group (p = 0.393). The morning surge of the SBP was 14 ± 11 mmHg for the normotensive and 15 ± 11 mmHg for the WCH group (p = 0.814). The PP means were 50 ± 6.0 mmHg and 55 ± 8.0 mmHg for the normotensive and WCH groups, respectively (p = 0.074).

Table 3 shows the distribution of the sample in relation to the nocturnal dipping of SBP and it can observed an impairment of the dipping, with a predominance of attenuation, followed by absent dipping.

Figure 1 shows the 24-hour hourly means of BP in the WCH and normotensive groups. The elderly women with WCH presented higher SBP means in the first hours of the morning (8 am to 12 pm), when compared to the normotensive ones (133 ± 8 *vs* 123 ± 9, respectively, p < 0.001).

In the two groups, the mean SBP and DBP levels were higher during the morning period, between 8 am and 12 pm, with a peak around 10 am, which later decreased between 12 pm and 3 pm, which comprehends the postprandial period, rising again at 3 pm and maintaining a plateau until 10 pm. After 10 pm, they decreased to a lowest point between midnight and 2 am and again increased up to the first hours of the morning.

No significant differences were observed during the nocturnal period (the two groups presented a decrease in SBP and DBP from the wakefulness to the sleep period), in the morning surge (both groups presented SBP and DBP increase from the lowest level during sleep to the period up to two hours after waking up) and in the postprandial period (SBP decrease up to two hours after lunch). A positive correlation was observed between age and BMI with the SBP

Table 1 - Clinical characteristics of the patients stratified as normotensive and white-coat hypertensive individuals

	Normotensive	White-coat hypertensive	p	X^2
Nº	19	17		
Age (yrs)	69.2 ± 7.0	69.8 ± 7.0	0.778	
Smoker	5%	5.8%		0.0139
Snorer	58.9%	62.5%		0.0466
Coffee-drinker	26.3%	31.3%		0.1036
Weight (kg)	63.2 ± 11.4	65.2 ± 8.3	0.545	
Height (m)	1.57 ± 6.07	1.59 ± 4.55	0.252	
BMI (W/h²)	25.9 ± 4.05	25.9 ± 3.33	0.968	

BMI - body mass index; W - weight; h² - square height; kg - kilograms; m - meters.

Table 3 - Classification according to the nocturnal dipping of the systolic arterial pressure in the normotensive and white-coat hypertensive groups

Nocturnal dipping	Normotensive (n = 19)	White-coat (n = 17)
Present	4 (21.1%)	6 (35.3%)
Absent	5 (26.3%)	4 (23.5%)
Attenuated	10 (52.6%)	7 (41.2%)

Fisher's exact test (p = 0.689).

Table 2 - Means of the systolic and diastolic pressures and of the arterial pressure range at the medical office and during wakefulness, sleep and 24-hour measurement for the normotensive and white-coat hypertensive patients

	Systolic blood pressure			Diastolic blood pressure		
	Normotensive	White-coat	p	Normotensive	White-coat	p
Values (mmHg)						
Office	128.32 ± 11.2	152.88 ± 11.9	< 0.001	76.05 ± 8.37	87.05 ± 11.1	0.002
24-hour	119.89 ± 7.81	122.4 ± 5.39	0.275	69.84 ± 7.59	68 ± 7.2	0.462
Wakefulness	121 ± 8.46	124.35 ± 6.12	0.187	71.78 ± 7.67	69.82 ± 7.85	0.454
Sleep	114.57 ± 9.95	113.8 ± 8.79	0.808	62.36 ± 8.87	59.82 ± 6.83	0.346
Range						
24-hour	10.2 ± 3.4	12.5 ± 3.8	0.072	8.2 ± 2.3	9.2 ± 2.3	0.214
Wakefulness	8.8 ± 3.7	12.2 ± 4.7	0.022	6.9 ± 2.7	8.4 ± 2.7	0.108
Sleep	9.5 ± 3.9	7.9 ± 2.3	0.152	6.9 ± 2.5	6.1 ± 2.3	0.318

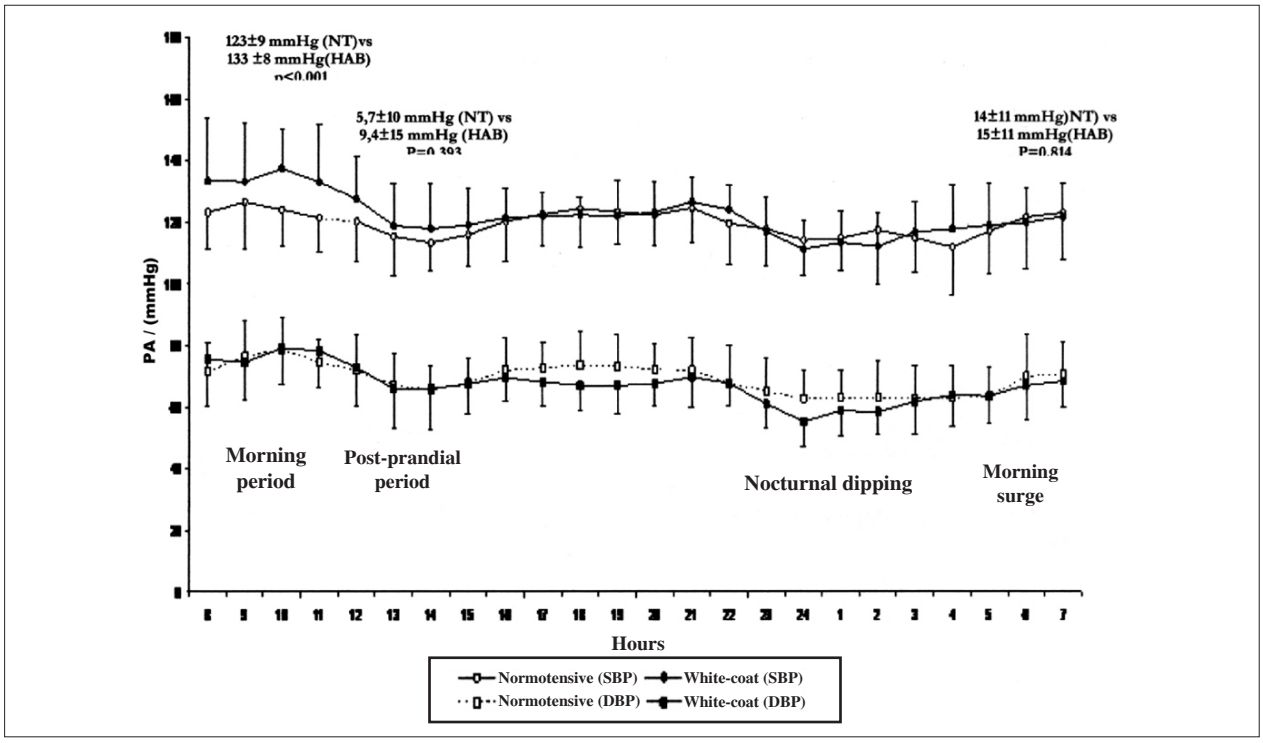

Figure 1 - Temporal means of the systolic (SBP) and diastolic (DBP) arterial pressures of elderly normotensive and white-coat hypertensive individuals.

means during the nocturnal period in the WCH group (r = 0.578, p = 0.015 and r = 0.488, p = 0.055, respectively), which was not observed in the normotensive group (Figures 2 and 3).

Discussion

The present study shows that the BP does not behave in the same way in normotensive female elderly patients and female elderly patients with white-coat hypertension. When assessed

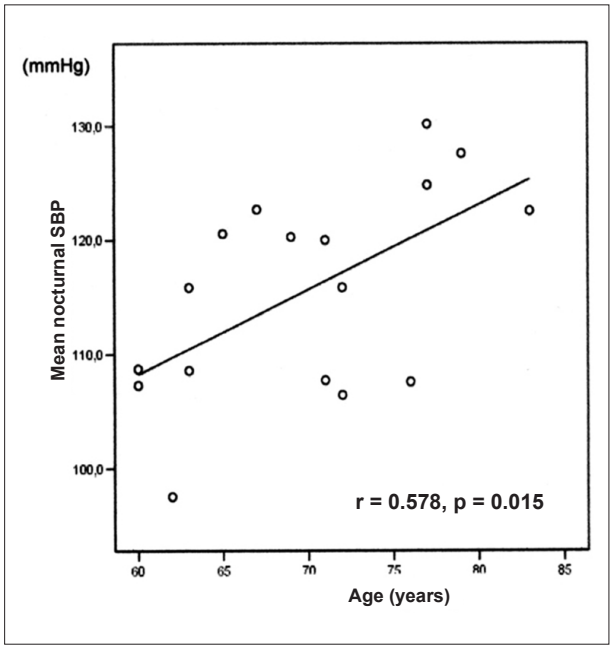

Figure 2 - Association between age and SBP means in the nocturnal period in elderly women with WCH.

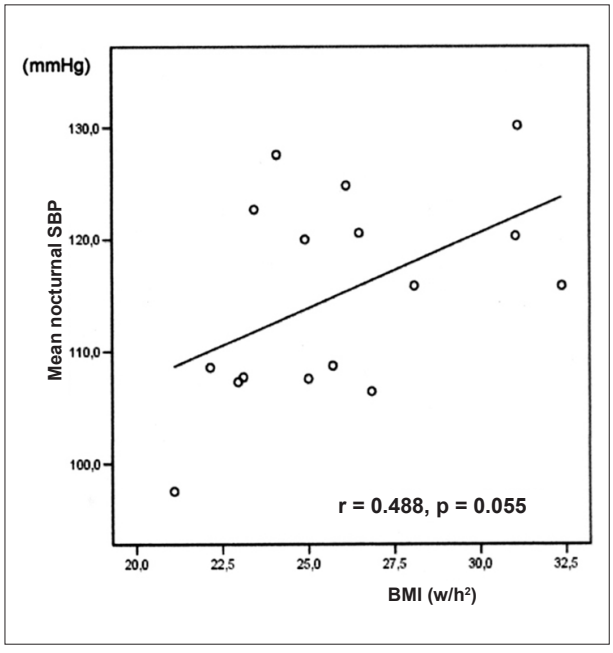

Figure 3 - Relação entre o IMC e as médias de PAS no período noturno nas idosas com HAB.

through ABPM, the blood pressures in the morning period differed between the normotensive and the WCH groups, with the latter presenting significantly higher SBP levels. This behavior had not been reported in elderly women and can justify the previously described alterations in ventricular wall mass and thickness, corroborating the hypothesis that it is not a benign entity[8,14,15].

However, we observed that the 24-hour means of SBP and DBP were similar in the two groups. Evidence has shown several alterations between normotensive individuals and individuals with WCH.

Considering the literature, this seems to be the first study that demonstrated a difference in the behavior of ABPM in elderly women with WCH, when compared to normotensive elderly women; however, these findings might not be exclusive for this sex and age range.

The prognostic relevance of WCH remains controversial. Most studies suggest that individuals with WCH present a higher cardiovascular risk than the normotensive individuals, although lower than that of individuals with sustained arterial hypertension[16-18].

The study by Verdechia et al[19] analyzed the incidence of cerebrovascular accident during a 10-year period of follow-up. The main finding was that WCH was associated to a low risk, similar to that presented by true normotensive individuals, during the five first years of follow-up. However, after this period, the risk increased and became the same presented by the true hypertensive individuals[19].

Different explanations for this intermediate risk profile of WCH have been proposed, such as the increase in the BP variability, the increase in the sympathetic nervous activity and more oxidative stress[20-27].

Neumann et al[28] carried out a study with men aged 40 to 70 years, which objective was to determine whether individuals with WCH showed evidence of autonomic deregulation similar to that found in patients with sustained hypertension[28]. It was observed that the individuals with WCH presented higher sympathetic activation and a significantly lower parasympathetic tonus than normotensive individuals, although similar to individuals with sustained hypertension. They concluded that these similarities between persistent hypertension and WHC, reflecting the attenuated parasympathetic control of the heart - that is, an autonomic deregulation - could constitute one of the mechanisms for increased risk of cardiovascular events in the affected individuals[28].

Our study showed that the variability presented a statistically significant difference between the groups during the wakefulness period, being higher in the WCH group. The WCH seems to be a condition with a generalized BP hyper-reactivity and although the BP means at the ABPM are normal, the increase in the variability, when present, can be potentially harmful to the cardiovascular system in elderly individuals[28,29].

The SBP has been considered a better predictor of cardiovascular outcomes than the DBP[30]. We found a positive correlation between age and BMI with the SBP means during the nocturnal period in the group of elderly women with WCH, a fact that was not observed in the normotensive group. Dolan et al[7] did not observe an association between BMI and WCH in their study[7].

In our study, the women with WCH presented higher SBP means in the first hours of the morning, when compared to the normotensive women. We also verified, in the two groups, an obvious circadian rhythm of blood pressure, with higher SBP and DBP levels during the wakefulness period, decreasing during the sleep period at night and a gradual increase during the night until the first hours of the morning.

Many elderly individuals older than 70 years and individuals of African ethnicity do not exhibit a nocturnal dipping in BP[31]. It has also been demonstrated that the elderly present a lower nocturnal dipping of BP when measured in mmHg, or as a BP proportion during 24 hours[32].

Staessen et al[32] reported that the probability of presenting an attenuated or absent nocturnal dipping increased 2.8-fold from 30 to 60 years and 5.7-fold from 60 to 80 years[32]. The explanations proposed for these observations include the fact that the elderly spends more time in bed than younger people, experiences less deep sleep wakes up more often at night and has a more fragmented sleep[33]. The elderly also present a higher morning surge of BP than younger individuals, and throughout time, particularly when they present sustained arterial hypertension, they will tend to develop more areas of potential ischemia in the brain (shadow areas), in the heart, kidneys and peripheral vessels. Finally, elderly individuals present a higher absolute risk of cardiovascular events than younger individuals, not only due to the age, but attributable in part, to sleep apnea, with consequent cardiac arrhythmias, which are more common among individuals older than 65 years[33].

The incidence of most adverse cardiovascular events seems to follow a circadian pattern, reaching a peak in the morning, during and soon after waking up[34].

Studies have suggested that during the first hours after waking up, the phases of this cycle present a synchronization that creates a condition that predisposes to the rupture and thrombosis of atherosclerotic plaques in susceptible individuals, which would favor an increased cardiovascular risk during this period of the day. The morning surge of the BP can act as a trigger for cardiovascular events, including myocardial infarction and cerebrovascular accident[35]. However, in our sample, no differences were found regarding the morning surge between the groups.

The postprandial hypotension is a frequently observed phenomenon in patients with autonomic dysfunction, arterial hypertension and healthy elderly individuals and its prevalence increases with age[36]. It can cause clinical symptoms that include dizziness, an "empty-headed" sensation or syncope due to the impairment of brain perfusion[36]. Studies have demonstrated that elderly individuals with deep PPH presented a higher risk for future falls, syncope, coronary events and cerebrovascular accident. The total mortality in this group was also higher[37].

In our sample, the WCH group presented, on average, a decrease in the postprandial SBP of almost 4.0 mmHg higher than the normotensive group. Although the difference between the groups did not reach statistical significance, these few mmHg can represent an important clinical impact

in elderly individuals. The PPH can significantly increase the BP variability during the wakefulness period and also during the 24-hour period[11]. In our study, this finding was verified in the group with WCH during the diurnal or the wakefulness period, but not during the 24-hour period.

Kohara et al[38] also verified, in a sample of elderly individuals with SAH, that the higher the PPH, the higher the prevalence of asymptomatic cerebrovascular lesions evaluated through magnetic resonance and they found no correlation between the hypotension and the BP means during wakefulness and at night, or with the phenomenon of absence or attenuation of the nocturnal dipping[38].

The pulse pressure obtained by the ABPM and calculated by the difference between the 24-hour systolic and diastolic BP means has also shown to be a good prognostic indicator of events and values > 53 mmHg have shown to be related to an increase of almost 5-fold in the occurrence of cardiovascular outcomes[39]. The PP means in the group with WCH were higher than those observed in the normotensive group, which can also represent a clinical impact in this age range.

Observational studies, based on the calculation of PP and mean arterial pressure (MAP) of conventional BP readings suggest that, in middle-aged adults and the elderly, the cardiovascular prognostic worsens as the PP increases, but not the MAP[10].

Several difficulties were overcome in the present study, mainly during the handling of the elderly patients and the performance of several procedures in normal individuals. In spite of the small sample size, the study is absolutely original regarding its population and methodological characteristics, thus being of high scientific value.

Among the limitations of the present study is the fact that it did not include the measurement of biochemical parameters such as lipoprotein and glycemia levels; therefore, the impact of these risk factors cannot be measured. Target-organ lesions were not analyzed, either, such as left ventricular hypertrophy.

The sample consisted of Caucasian females; therefore, the results cannot be generalized.

Conclusion

Significantly higher SBP levels were detected from 8 AM to 12 PM in the women with WCH. The higher BP variability in the WCH group was observed during the wakefulness period.

No significant differences were observed between the two groups regarding the BP post-prandial decrease, morning surge and pulse pressure.

Recent evidence suggests that WCH can increase the risk of CVA. The present study open new perspectives for other determinants of cardiovascular risk in the spectrum of assessment of BP circadian rhythm in this population.

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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