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## Original Paper

# Assessment of Arterial Stiffness by 24-Hour Ambulatory Blood Pressure Monitoring in Nocturnal Hypertensive or Normotensive Subjects

Lucas Drucaroff<sup>a</sup> Agustín Ramirez<sup>c</sup> Ramiro Sanchez<sup>b</sup>  
Daniel P. Cardinali<sup>d</sup> Santiago Perez-Lloret<sup>e, f</sup>

<sup>a</sup>Departamento de Psiquiatría, Instituto de Investigaciones Neurológicas Raul Carrea, <sup>b</sup>Fundación Universitaria 'Dr. Rene G. Favaloro', <sup>c</sup>Sección Hipertensión, ICYCC, Fundación Favaloro, <sup>d</sup>Departamento de Docencia e Investigación, and <sup>e</sup>Laboratory of Epidemiology and Experimental Pharmacology, Institute for Biomedical Research (BIOMED), School of Medical Sciences, Pontifical Catholic University of Argentina (UCA), and <sup>f</sup>the National Scientific and Technical Research Council (CONICET), Buenos Aires, Argentina

## Key Words

Hypertension · Arterial stiffness · Gender · Aging

## Abstract

**Background:** Nocturnal hypertension, male gender, age and arterial stiffness are important risk factors for cardiovascular morbidity and mortality. The objective of this study was to assess arterial stiffness in nocturnal hypertensive or normotensive men and women >40 years of age. **Methods:** Twenty-four-hour ambulatory blood pressure monitoring was performed in 144 men and 137 women. Eighty-eight subjects were between 40 and 49 years old (53% men), 98 were between 50 and 59 years old (55% men) and 95 were >60 years old (45% men). They were classified as nocturnal hypertensive if their average night systolic blood pressure and/or diastolic blood pressure was >120/70 mm/Hg. Arterial stiffness was assessed by the Ambulatory Arterial Stiffness Index (AASI), which is calculated as 1 minus the slope of diastolic on systolic blood pressure during the 24-hour recording period. Results were analyzed by analysis of covariance and were adjusted for 24-hour mean arterial pressure, the presence of antihypertensive treatment, height and heart rate. **Results:** Women showed a higher AASI compared to men, independently of age. In men, the AASI increased with age, being higher in nocturnal hypertensive than in nocturnal normotensive subjects, independently of age. Nocturnal hypertensive women showed higher AASI values than their respective nocturnal normotensive controls in the 50- to 59-year and >60-year age groups only. **Conclusion:** The results show that arterial stiffness is higher among nocturnal hypertensive subjects, especially in women >50 years old.

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Dr. Santiago Perez-Lloret  
Laboratorio de Epidemiología y Farmacología Clínica  
Universidad Católica Argentina  
Av. Alicia Moreau de Justo 1600, C1107AAF, Buenos Aires (Argentina)  
E-Mail [santiagopl@conicet.gov.ar](mailto:santiagopl@conicet.gov.ar)

## Introduction

Age is an important risk factor for cardiovascular mortality [1, 2]. Although men have a higher lifetime cardiovascular risk, the age-related risk increase is steeper in women after the menopause compared to men [3, 4].

Arterial compliance is lower in the elderly [5, 6]. Deposition of collagen in the intimal layer of the arterial wall by smooth muscle cells results in progressive reduction in arterial compliance [7]. Metabolic changes leading to increased body weight, serum cholesterol and insulin resistance as well as to sympathetic nervous system overactivity and baroreceptor dysfunction contribute to the development of arterial stiffness in older adults [7]. This condition, affecting 15–25% of people >40 years of age, substantially increases the cardiovascular risk [7, 8].

Arterial stiffness is measurable by a number of techniques, including pulse-wave velocity and central or peripheral augmentation indexes [9]. Recently, the Ambulatory Arterial Stiffness Index (AASI) has been developed and validated [5, 10]. It is calculated from systolic (SBP) and diastolic blood pressure (DBP) recordings obtained by 24-hour ambulatory blood pressure monitoring (ABPM) [5]. The AASI is an independent predictor of cardiovascular mortality, especially of fatal stroke in ambulatory normotensives [10], suggesting that it may be an early indicator of arterial stiffness before sustained hypertension develops [11].

In addition, nocturnal hypertension is a significant predictor of cardiovascular mortality and has been demonstrated to be more accurate than daytime hypertension [12–14]. Blunted nocturnal blood pressure fall is related to the lack of appropriate nighttime parasympathetic activation and sympathetic inactivation [12, 13, 15]. Since endothelial dysfunction is common among nocturnal hypertensives [16] and an increased proinflammatory activity is demonstrable in this group [17], a connection between nocturnal hypertension and arterial stiffness can be postulated.

This study aimed to compare arterial stiffness, measured by the AASI, among men and women >40 years old suffering from nocturnal hypertension to that of healthy controls.

## Methods

### *Sample*

Two-hundred and eighty-one individuals >40 years old underwent ABPM. Subjects who suffered from terminal renal insufficiency, significant valvular disease, cardiomyopathy, uncontrolled diabetes, hypo- or hyperparathyroidism or congestive heart failure were not included in the study. People undergoing corticosteroid, antineoplastic, anticoagulant, insulin, oral antidiabetic or digitalic treatment were also excluded as well as those whose ABPM was shorter than 23 h or lacked two or more consecutive readings. None of the subjects worked during the nighttime hours or in shift work schedules.

Participants were divided according to age: 40–50 years old, 50–60 years old and >60 years old.

### *24-Hour ABPM*

Noninvasive ABPM was performed on a normal weekday by means of an automatic ABP monitor Spacelab 90207 (Spacelab Medical Inc., USA) validated by the Association for the Advancement of Medical Instrumentation (AAMI) and the British Hypertension Society (BHS) [18, 19]. The monitor was placed on the nondominant arm and set to take blood pressure and heart rate readings every 20 min from 06:00 to 22:00 h and every 30 min for the remaining time. Subjects were asked to complete a 24-hour diary during the day of the recording, which served to define daytime and nighttime periods.

**Table 1.** Sample characteristics

	40–49 years (n = 88)	50–59 years (n = 98)	>60 years (n = 95)	p value
Male	47 (53)	54 (55)	43 (45)	<0.3
BMI	27.7±4.8	26.9±3.5	27.3±4.3	<0.4
Height, cm	170±10	168±9	165±9*,#	<0.001
AASI	0.22±0.14	0.30±0.14*	0.36±0.13*,#	<0.001
Daytime BP				
Systolic	129.2±13.2	133.5±13.8*	135.4±11.2*	<0.004
Diastolic	84.9±10.5	86.1±10.0	81.2±7.5*,#	<0.001
Nighttime BP				
Systolic	114.0±12.1	115.8±14.5	120.1±12.6*	<0.006
Diastolic	69.4±9.7	69.8±10.4	67.6±8.5	<0.2
24-hour BP				
Mean BP	94.6±10.4	96.5±10.4	94.5±7.4	<0.2
Heart rate	76.6±8.3	73.7±8.7	71.8±10.9*	<0.002
Diurnal hypertension				
Untreated	25 (28)	32 (33)	15 (16)	<0.001
Treated	19 (22)	33 (23)	46 (59)	
Nocturnal hypertension	22 (25)	28 (29)	33 (35)	<0.3

Data are means ± SD or n (%). BMI = Body mass index.

\* p < 0.05, vs. the 40- to 49-year age group; # p < 0.05, vs. the 50- to 59-year age group (ANOVA followed by Bonferroni).

Patients were included in the diurnal normotensive group if their SBP/DBP was <135/85 mm Hg and they were not under antihypertensive treatment [20]. Nocturnal hypertension was defined as a nocturnal SBP >120 and/or a DBP >70 mm Hg [21].

#### *Ambulatory Arterial Stiffness Index*

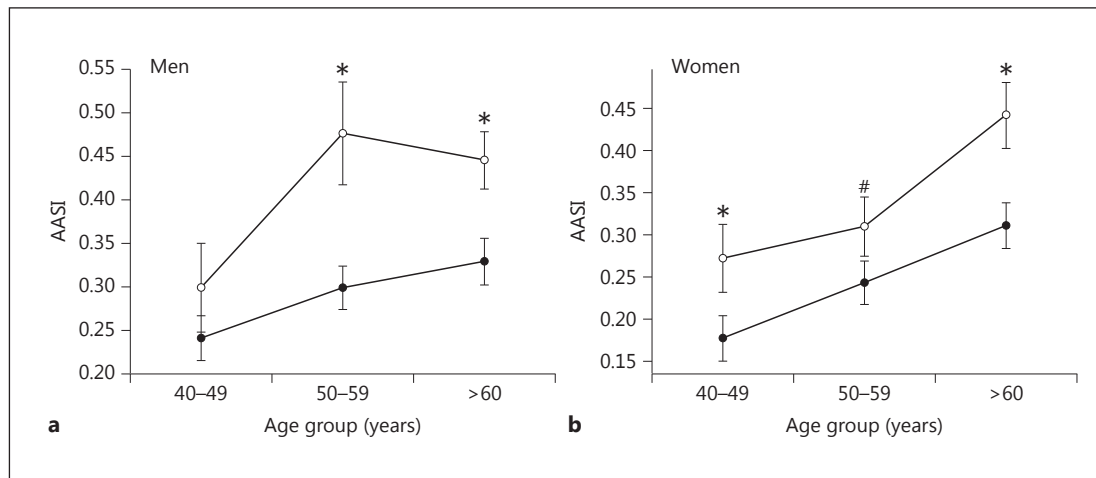
The AASI was calculated as 1 minus the slope of the DBP to SBP linear regression coefficient [5, 10]. The linear coefficient was obtained by the least squares technique. All the recordings from the 24-hour study span were included in the regression.

#### *Statistical Analysis*

An analysis of variance and a  $\chi^2$  test were employed to compare the variables among the studied groups. An analysis of covariance (ANCOVA) was used to analyze differences in the AASI according to sex, age and occurrence of nocturnal hypertension, independently from the covariates (24-hour mean blood pressure, antihypertensive treatment, heart rate and height).

## Results

The mean age ( $\pm$  SD) of the 281 studied subjects was  $56 \pm 10$  years. Fifty-seven percent of the subjects were diurnal hypertensives. The prevalence of nocturnal hypertension was 46% in diurnal hypertensives and 7% in normotensives. Other characteristics of the studied sample are summarized in table 1. The AASI correlated positively with age ( $p < 0.001$ ) and 24-hour SBP ( $p < 0.01$ ) and negatively with 24-hour DBP. Height was not associated with the AASI.



**Fig. 1.** The AASI in men (a) and women (b) >40 years old. The difference between nocturnal normotensive (●) and hypertensive (○) subjects was evaluated by ANCOVA adjusted for 24-hour mean arterial pressure, heart rate, height and antihypertensive treatment. \*  $p < 0.05$ ; #  $p < 0.06$ . Data shown are means  $\pm$  SEM.

Women showed a higher AASI compared to men (mean  $\pm$  SEM,  $0.32 \pm 0.01$  vs.  $0.27 \pm 0.01$ , respectively;  $p < 0.02$ ), independently of age. In men, ANCOVA indicated that the AASI was higher in the older groups (40–49 years:  $0.22 \pm 0.02$ ; 50–59 years:  $0.27 \pm 0.03$ ; >60 years:  $0.38 \pm 0.02$ ;  $p < 0.001$ ) and in the nocturnal hypertensive subjects compared to nocturnal normotensives, independently of age ( $0.33 \pm 0.02$  and  $0.24 \pm 0.02$ , respectively;  $p < 0.01$ ; fig. 1). In contrast, the AASI was higher in nocturnal hypertensive women in the 50- to 59-year age group (nocturnal hypertensives:  $0.47 \pm 0.06$ ; normotensives:  $0.30 \pm 0.02$ ;  $p < 0.05$ ) and in the >60-year age group (nocturnal hypertensives:  $0.45 \pm 0.03$ ; normotensives:  $0.33 \pm 0.03$ ;  $p < 0.05$ ) but not in the 40- to 49-year age group (nocturnal hypertensives:  $0.29 \pm 0.05$ ; normotensives:  $0.24 \pm 0.02$ ;  $p < 0.1$ ), as observed in figure 1.

## Discussion

Foregoing results indicate that the AASI increased with age and was higher in nocturnal hypertensive subjects. A distinctive pattern of the AASI was found in men and women. Nocturnal hypertensive males showed a higher AASI, independently of age. On the contrary, only nocturnal hypertensive women >50 years old showed a higher AASI compared to nocturnal normotensive women, whereas no such difference was found in the younger group.

The AASI is a new index of arterial stiffness that correlates accurately with most frequently used methods for measuring arterial stiffness. Indeed, it may outdo them mainly because it is performed along a regular day and in the individual's natural environment [5]. The AASI may depend on the mechanical properties of small arterioles [11].

Arterial stiffness depends on the artery characteristics (i.e. wall structure, function and lumen size) and the distending pressure [5, 22]. As the BP changes during the 24-hour span, the AASI is capable of evaluating arterial stiffness with varying distending pressures.

The AASI is a powerful predictor of total cardiovascular and stroke mortality [10] and is clearly superior to pulse pressure. Recently, the AASI has been shown to be a good predictor of end-organ damage, such as renal damage, microalbuminuria, left ventricular hypertrophy

and carotid abnormalities in untreated hypertensive individuals [23, 24]. These results suggest that the AASI should be taken into account when evaluating cardiovascular risk.

In our study, the AASI was higher among nocturnal hypertensive subjects. It could be argued that these results are related to increased 24-hour blood pressure, as an increased distending pressure would produce arterial stiffness [22]. However, ANCOVA allowed us to control any possible effects of the differences in the average mean arterial pressure and anti-hypertensive treatment among the age and sex groups, ruling out that possibility.

Nocturnal hypertension is a significant independent cardiovascular risk factor, even more powerful than daytime elevated blood pressure [12, 14]. In support of the present results, the lack of a nocturnal BP fall has been related to the thickening of the intimal layer of the common carotid artery, which reduces its distensibility [25, 26]. Nocturnal hypertensive subjects showed an increase in some indexes of endothelial damage (e.g. ICAM-1 and von Willebrand factor) and hypercoagulability (D-dimer and plasminogen activator inhibitor), independently from daytime blood pressure values [17]. These data support the hypothesis that in nocturnal hypertensive subjects, vascular intimal fibrosis can result from endothelial damage, which reduces vessel distensibility.

The findings that nighttime hypertension was not associated with an increased AASI in women <40 years old can be related to the ovarian cycle status. Estrogenic deprivation in the postmenopausal period is related to significant deterioration in endothelial function and arterial stiffness, which can be reverted by a hormone replacement therapy [27, 28]. Moreover, the postmenopausal period is associated with a change in the salt sensitivity status, leading to increased volume load, arterial stiffness and nocturnal hypertension [28–30], supporting the results herein reported. Although women's hormonal status could not be evaluated in this study, it can be assumed that after 50 years of age, most women are already postmenopausal [31]. Antihypertensive treatment reduces arterial stiffness by two major mechanisms [32]. By lowering peripheral resistance, it lowers the intra-arterial volume with a concomitant reduction in the arterial stiffness [32]. Additionally, by interfering with systems involved in the vascular growth control (e.g. the renin-angiotensin system), a reduction in arterial fibrosis occurs, therefore increasing the vessel's distensibility [32, 33].

In summary, nocturnal hypertension was related to an increase in arterial stiffness in men of all ages and in women >50 years old. Thus, it would be advisable to monitor arterial stiffness periodically in nocturnal hypertensive patients. The AASI comes at no cost with 24-hour ABPM and is a significant cardiovascular morbidity and mortality predictor, making it the best choice for arterial stiffness evaluation and follow-up.

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