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ORIGINAL ARTICLE

Association between 24-hour ambulatory heart rate and arterial stiffness

P Albaladejo[1], R Asmar[2], M Safar[1] and A Benetos[1]
[1]*Department of Internal Medicine and INSERM, U337, Hôpital Broussais, Paris, France;* [2]*Institut de Recherche et de Formation Cardiovasculaire, Paris, France*

Clinical and experimental studies point to a positive association between carotid-femoral pulse wave velocity (PWVcf) and casual heart rate. However, an association with 24-h ambulatory heart rate has never been investigated. Twenty-four hour ambulatory heart rate and PWVcf (automatic computerised technique) were simultaneously measured in 213 subjects with untreated mild-to-moderate essential hypertension. It was found that mean ambulatory heart rate was higher in women than in men but the difference reached statistical significance only in those below 50 years of age during night-time measurements. As well as age and blood pressure, 24-h ambulatory heart rate was also an independent factor influencing PWVcf. Independent of gender, the relationship between PWVcf and ambulatory heart rate was stronger in patients over 50 years of age. Casual heart rate was not a significant determinant of PWVcf in this population. In conclusion, ambulatory heart rate contribution to explain pulse wave velocity is more important than casual heart rate. The relationship between 24-h heart rate and pulse wave velocity is stronger for subjects older than 50 years of age independent of gender.
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Introduction

Epidemiologic studies have shown that heart rate is a risk factor for cardiovascular[1,2] and non-cardiovascular death.[2,3] Compelling evidence has been accumulated that heart rate can contribute to the progression of coronary atherosclerosis.[4–6] The predictive role of heart rate on cardiovascular morbidity was observed primarily in hypertensive men.[7] This finding suggests that heart rate and blood pressure might act synergistically in the development of cardiovascular complications.

Hypertension in young people is typically associated with elevated heart rate and cardiac output.[8] In recent years, several studies have shown that accelerated heart rate is an independent precursor of hypertension.[9,10] However, some studies have shown that after adjustment for blood pressure, the role of heart rate was not significant in the development of future hypertension.[10] The relationship between heart rate and blood pressure has been established in large cohorts of unselected subjects.[9] Sa Cunha *et al*[11] have shown that pulse wave velocity and casual heart rate at rest were positively correlated in normotensive and hypertensive patients. The same authors have also shown that ambulatory heart rate is related to pulsatile changes in the diameter of the carotid artery.[12] Asmar *et al*[13] have shown that heart rate measured over 2 h was also positively related to pulse wave velocity in a small cohort of hypertensive patients. However, there are no data comparing the relation between aortic distensibility and heart rate assessed during an ambulatory measurement for a period of 24 h.

The aim of the present study was to evaluate the influence of heart rate measured casually and during daytime, night-time and 24 h, on pulse wave velocity in a cohort of subjects with mild-to-moderate hypertension.

Patients and methods

In the present study, we present data that describe 213 consecutive patients presenting with untreated mild-to-moderate hypertension. All these subjects had personal history of high blood pressure and were examined in the out-patient hypertension clinic of Broussais Hospital, France. Only patients with clinical signs of secondary hypertension were excluded from the study. Subjects presenting normal blood pressure values the day of the examination were included in the study. This cohort was composed of 130 men and 83 women aged 16 to 74 years.

Casual blood pressure was measured after a 15-min rest in the supine position, using a mercury sphygmomanometer. An average of three measurements were taken for each patient. Korotkoff phase I sounds were used for the determination of systolic blood pressure (SBP) and phase V for diastolic blood pressure (DBP). Casual heart rate was clinically assessed by averaging two pulse counts of 1 min each.

Correspondence: Dr Athanase Benetos, Hôpital Broussais, 96 rue Didot, 75674 Paris Cedex 14, France
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Automated blood pressure monitoring was carried out in each patient using a DIASYS model 200R monitor (Novacor®, Rueil Malmaison, France) to measure and record blood pressure and heart rate over a full 24-h period.[14] The high reliability of this method has been discussed previously.[15] Recordings were performed every 15 min throughout the 24-h period. Ambulatory monitoring was undertaken for a full active day; the patient worked as usual during the day and then went home in the evening. Recordings showing a calculated pulse pressure >100 mm Hg, or <20 mm Hg with SBP >100 mm Hg were deleted before further data analysis. Each full day recording was divided into a diurnal period (07.00 to 22.00) and a nocturnal period (22.00 to 07.00). Mean values of systolic, diastolic, pulse pressure and heart rate for diurnal (dSBP, dDBP, dPP, dHR, respectively), nocturnal (nSBP, nDBP, nPP, nHR, respectively) and 24-h (24SBP, 24DBP, 24PP, 24HR, respectively) were used for statistical analysis.

Carotid to femoral pulse wave velocity (PWVcf) was measured using an automatic computerised technique (Complior®, Colson, France). This method has been described previously.[16] Briefly, two pressure waves were recorded transcutaneously at two sites (at the base of the neck for the common carotid artery and over the right femoral artery). PWVcf is measured using an algorithm based on the time-shifted and repeated linear correlation calculation between the initial rise in pressure waveforms. Height was measured at the time of examination.

Standard statistical analysis was performed using a Statview 5 software (SAS Institute Inc, Cary, NC, USA) running on a PC compatible computer. Values are expressed as means ±1 standard deviation. Simple regression analyses were performed by standard methods. Stepwise multiple regression analyses were performed to assess relations of covariates. In all models, age was systematically introduced as an independent continuous variable. The significance level was fixed at 0.05.

Results

Table 1 summarises the clinical characteristics of the population studied. The cohort was divided according to gender and to classes of age (>49 and <50 years). A difference in heart rate was noted between men and women aged less than 50 years. In women younger than 50 years, heart rate was constantly 2 to 4 bpm higher than in men of the same age. However, this difference was significant only for nocturnal measurements. Blood pressure was higher in men than in women aged less than 50 years. This difference was not significant for nocturnal DBP. In subjects older than 49 years, systolic and diastolic blood pressure was constantly higher in men than in women. However, this difference was significant only for diastolic pressure. PWVcf was higher in subjects older than 50 years, whatever the gender.

Table 2 shows the results of a stepwise regression analysis to explain PWVcf by age, gender, height, systolic pressure and heart rate during casual and ambulatory measurements. During daytime, night-time and 24-h measurements, respectively 26.6, 26 and 27.1% of PWVcf variance was explained by the regression when age, height, SBP and heart rate were included as covariates.

Table 3 indicates the correlation coefficients of the relationship between ambulatory heart rate and corresponding systolic, diastolic, pulse pressure and PWVcf according to age and gender. The correlations between PWVcf and heart rate during 24 h were stronger in women and men older than 50 years. In women older than 50 years, diurnal and 24-h heart rate are related to systolic and diastolic blood pressure. In men older than 50 years, the relationship between blood pressure and diurnal and 24-h heart rate was significant only for DBP. In younger subjects, the relation between heart rate and blood pressure was weak. During the night-time, poor correlations were observed between heart rate and blood pressure.

Figure 1 shows a positive relation ($r = 0.146$, $P < 0.05$) between pulse wave velocity and 24-h heart rate.

Discussion

This study has shown that: (1) ambulatory heart rate contribution to explain pulse wave velocity is more important than casual heart rate, and (2) the relationship between 24-h heart rate and pulse wave velocity is stronger for subjects older than 50 years independent of the gender.

As for ambulatory blood pressure, this study shows that ambulatory heart rate is an important determinant of alteration of aortic distensibility.[13] Ambulatory heart rate significantly contributed to explain the regression with PWV in a model including age, gender, height and SBP. Heart rate during activity may be an important prognostic factor of arterial alteration, however, nocturnal relations between heart rate and pulse wave velocity are similar to diurnal and 24-h measurements in our study. Mancia *et al*[17] have shown that blood pressure and heart rate vary directionally in a similar manner during daily activities. Previous studies have shown that 24-h variabilities of heart rate and blood pressure are mainly determined by sympathetic and parasympathetic activity.[18] Thus, a coherent pathogenic link between heart rate and high blood pressure may be sympathetic activity or overactivity.[9]

In our study, the relationship between pulse wave velocity and heart rate was stronger in older subjects during ambulatory measurements. We did not observe an effect of gender in the relation between heart rate and pulse wave velocity. However, the small size of each subgroup may explain the weakness of the relationship observed between heart rate and pulse wave velocity.

Previous studies have investigated the association between heart rate and arterial rigidity. Bergel *et al*[19] have shown in *in vitro* studies that aortic dynamic elastic modulus is larger than static modulus. In anesthetized normotensive rats, Glaser *et al*[20] showed that dynamic compliance was lower than static compliance at any given mean arterial pressure. When tachycardia is induced by atrial pacing,

Table 1 Description of the cohort according to age and gender

	Women		Men	
	Age <50 yrs	*Age >49 yrs*	*Age <50 yrs*	*Age >49 yrs*
n	52	31	68	62
Age	40 ± 9	60 ± 8‡	40 ± 9	58 ± 6
Weight (kg)	66 ± 13	63 ± 12	80 ± 12#	81 ± 11#
Height (cm)	163 ± 7	162 ± 7	175 ± 7#	173 ± 7#
Body mass index (kg/m^2)	25 ± 6	24 ± 4	26 ± 4	27 ± 3#
HR	73 ± 10	69 ± 9	71 ± 14	70 ± 13
SBP	146 ± 22	157 ± 23†	157 ± 17*	157 ± 23
DBP	91 ± 15	92 ± 14	98 ± 13*	96 ± 15
PP	55 ± 14	65 ± 15§	60 ± 10	62 ± 15
dHR	83 ± 9	78 ± 10†	79 ± 13	77 ± 11
dSBP	139 ± 14	144 ± 17	150 ± 13#	150 ± 19
dDBP	93 ± 10	90 ± 11	98 ± 12°	96 ± 12°
dPP	45 ± 8	54 ± 11‡	52 ± 7#	55 ± 12
nHR	72 ± 10	67 ± 7†	68 ± 11°	67 ± 10
nSBP	122 ± 15	128 ± 16	131 ± 15*	134 ± 17
nDBP	77 ± 11	76 ± 10	80 ± 12	83 ± 11*
nPP	44 ± 9	52 ± 10‡	50 ± 7#	52 ± 10
24HR	79 ± 8	74 ± 9†	75 ± 12	74 ± 10
24SBP	132 ± 14	139 ± 17	143 ± 13#	145 ± 18
24DBP	87 ± 10	85 ± 11	91 ± 11°	91 ± 11°
24PP	45 ± 8	54 ± 10‡	52 ± 6#	53 ± 11
PWVcf (m/s)	10.5 ± 2.2	13.4 ± 3.8‡	11.6 ± 2.8°	12.7 ± 2.9†

Values are mean ± 1 s.d. SBP, casual systolic blood pressure; DBP, casual diastolic blood pressure; PP, casual pulse pressure; HR, casual heart rate; dSBP, mean of daytime systolic blood pressure; dDBP, mean of daytime diastolic blood pressure; dPP, mean of daytime pulse pressure; dHR, mean of daytime heart rate; nSBP, mean of night-time systolic blood pressure; nDBP, mean of night-time diastolic blood pressure; nPP, mean of night-time pulse pressure; nHR, mean of night-time heart rate; 24SBP, mean of 24-h systolic blood pressure; 24DBP, mean of 24-h diastolic blood pressure; 24PP, mean of 24-h pulse pressure; 24HR, mean of 24-h heart rate; PWVcf, pulse wave velocity between carotid and femoral arteries.
†$P < 0.05$, §$P < 0.01$, ‡$P < 0.001$ *vs* age <50 years, same gender; °$P < 0.05$, *$P < 0.01$, #$P < 0.001$ *vs* women, same age.

Table 2 Multiple linear analysis of aortic pulse wave velocity by age, gender, height, casual, daytime, night-time and 24-h systolic blood pressure and heart rate in all subjects

Independent variables	*Dependent variable (PWVcf)*			
	Casual	*Diurnal*	*Nocturnal*	*24-h*
Age	0.408	0.425	0.379	0.414
Gender	—	—	—	—
Height	0.148	0.137	0.128	0.132
SBP	0.151	0.167	0.211	0.184
HR	—	0.181	0.165	0.180
R^2 (%)[a]	22.5	26.6	26	27.1

Values are partial correlation coefficients of variables remaining at the last step of the analysis. SBP, systolic blood pressure; HR, heart rate.
[a]Percentage of variance explained, $P < 0.01$.

carotid distensibility decreases acutely but not femoral distensibility.[21]

Resting heart rate has been correlated with systolic and diastolic blood pressure in several studies. Usually, heart rate has a stronger correlation with systolic than with diastolic blood pressure with correlation coefficients ranging from 0.15 to 0.32.[9] We observed that with ambulatory measurements of blood pressure as well as heart rate, a correlation appears in this small population of hypertensive subjects. This relation between heart rate and blood pressure seems different depending on age, gender, and period of measurement. In women older than 50 years, diurnal and 24-h heart rate are related to systolic and diastolic blood pressure (the absence of significance for 24-h diastolic pressure is probably due to the small number of subjects in this subgroup). In men older than 50 years, the relation with diurnal and 24-h heart rate was significant only with DBP. In younger subjects, the relation between heart rate and blood pressure was weak. In the Chicago epidemiologic studies, heart rate showed a stronger relation to the level of the DBP.[22]

In the study of Palatini *et al*,[23] the association between ambulatory heart rate and blood pressure was weaker than casual measurements in two populations of normotensive and hypertensive subjects. This discrepancy may be due to the fact that, in normotensive subjects, heart rate was lower and a small number of subjects had a high heart rate. In the hypertensive group (HARVEST[23]), patients were younger, explaining the weaker relation between heart rate and blood pressure as observed in our study.

The exact mechanisms to explain the relation between heart rate and pulse wave velocity is still unclear and different hypothesis may be proposed. First, permanent accelerated heart rate which is better evaluated in 24-h ambulatory measurement may increase systolic stress and contribute to the arterial fatigue promoting arterial stiffness. Second, both heart rate and pulse wave velocity are influenced by

Table 3 Correlation coefficient of daytime, night-time and 24-h measurements of heart rate and systolic, diastolic, pulse pressure and carotido femoral pulse wave velocity according to age and gender

dHR	*dSBP*	*dDBP*	*dPP*	*PWV cf*
Women, age <50 years	0.04	0.07	0.02	0.18
Women, age >49 years	0.45*	0.44*	0.29	0.31
Men, age <50 years	0.089	0.19	0.17	0.17
Men, age >49 years	0.20	0.34**	0.03	0.24
nHR	*NSBP*	*nDBP*	*nPP*	
Women, age <50 years	0.11	0.21	0.07	0.20
Women, age >49 years	0.21	0.07	0.28	0.41*
Men, age <50 years	0.22	0.24*	0.05	0.17
Men, age >49 years	0.08	0.13	0.01	0.23
24HR	*24SBP*	*24DBP*	*24PP*	
Women, age <50 years	0.07	0.12	0.02	0.18
Women, age >49 years	0.40*	0.34	0.32	0.39*
Men, age <50 years	0.11	0.20	0.16	0.15
Men, age >49 years	0.18	0.31*	0.02	0.27*

Values are correlation coefficients. SBP, casual systolic blood pressure; DBP, casual diastolic blood pressure; PP, casual pulse pressure; HR, casual heart rate; dSBP, mean of daytime systolic blood pressure; dDBP, mean of daytime diastolic blood pressure; dPP, mean of daytime pulse pressure; dHR, mean of daytime heart rate; nSBP, mean of night-time systolic blood pressure; nDBP, mean of night-time diastolic blood pressure; nPP, mean of night-time pulse pressure; nHR, mean of night-time heart rate; 24SBP, mean of 24-h systolic blood pressure; 24DBP, mean of 24-h diastolic blood pressure; 24PP, mean of 24-h pulse pressure; 24HR, mean of 24-h heart rate; PWVcf, carotid to femoral pulse wave velocity.
$*P < 0.05$; $**P < 0.01$.

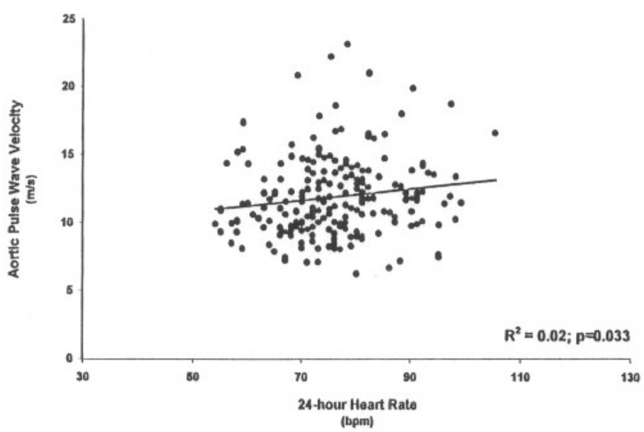

Figure 1 Aortic pulse wave velocity *vs* 24-h heart rate.

common factors such as an increased sympathetic overactivity. We can also suggest that arterial stiffness may alter baroreflex sensitivity explaining an increase in heart rate in subjects with increased pulse wave velocity (especially in older patients).

Twenty-four hour ambulatory heart rate has a stronger influence on aortic pulse wave velocity than casual heart rate measurements. This relationship is more pronounced for older subjects. The relevance of this finding in cardiovascular epidemiology remains to be explored.

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