Arterial distensibility and circadian blood pressure variability

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Objective To analyse the relationships between arterial distensibility and blood pressure level and its circadian variability assessed by non-invasive ambulatory blood pressure monitoring.

Design One hundred and six patients (69 men, 37 women; aged 20–72 years) without any cardiovascular complication or treatment underwent 24 h ambulatory blood pressure monitoring. Aortic distensibility was evaluated by carotid–femoral artery pulse-wave velocity measurements performed with a validated automatic device (Complior).

Results The pulse-wave velocity correlated significantly with age ($P < 0.001$), systolic blood pressure ($P < 0.01$) and heart rate ($P < 0.05$). Subjects with higher pulse-wave velocities (above the median value) had higher ambulatory blood pressure and heart rate values, mainly during night-time, and present a smaller nocturnal fall both in systolic and in diastolic blood pressure than do those with lower pulse-wave velocities (below the median). The pulse-wave velocity was revealed to be an independent predictor of the nocturnal fall in systolic blood pressure (multiple $r = 0.272$, $P < 0.02$) whereas age and, to a lesser extent, mean 24 h diastolic blood pressure were independent predictors of the nocturnal fall in diastolic blood pressure (multiple $r = 0.387$, $P < 0.001$).

Conclusion Reductions in arterial distensibility are associated with increased blood pressure and heart rate levels whereas perturbations of the circadian blood pressure profile are associated with increased nocturnal values. The increased risk of end-organ damage and vascular events in the presence of higher nocturnal blood pressure values suggests that a study of arterial distensibility in the normal follow-up of hypertensive patients might be of benefit.

Blood Pressure Monitoring 1996, 1:333–338

Keywords: blood pressure, circadian variability, arterial distensibility

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Received 15 February 1996 **Revised** 28 June 1996
Accepted 28 June 1996

 ISSN 1359-5237

Introduction

Blood pressure is known to be spontaneously variable in human beings. This variation has several sources: some of them are cyclical, whereas others are non-cyclical. Non-cyclical sources are represented by variations in posture, activity and emotional state. Cyclical sources include respiratory oscillation of blood pressure [1], ultradian rhythms and circadian variations [2].

Among the cyclical variations, the circadian blood pressure profile has attracted increasing attention. Normally, in normotensive subjects [3] and in the majority of essential hypertensive patients [4], the mean blood pressure declines by approximately 15% from day to night. Disturbances of the circadian cyclical variation may have clinical relevance both for diagnosis and for prognosis. Reductions in circadian blood pressure variation have been described in some forms of secondary hypertension [5]. Patients with reduced nocturnal falls in blood pressure, 'non-dippers', more frequently have strokes [4] and may be at increased risk of target-organ damage and, perhaps, cardiovascular complications in subsequent years relative to subjects with a normal day–night blood pressure rhythm, 'dippers' [6–8]. Since cardiovascular morbidity and mortality of hypertensive patients are related mainly to lesions of the large arteries and since several studies showed that, in hypertension, not only the resistive vessels but also the large arteries are affected [9,10], we described the relationships between arterial distensibility and blood pressure level determined according to different methods [11]. Since the highest linear correlation coefficient was noted with the ambulatory blood pressure monitoring averages, in the present study we focused on the possible relationships between

arterial distensibility evaluated by pulse-wave velocity and the circadian blood pressure variability evaluated by 24 h non-invasive ambulatory blood pressure monitoring.

Patients and methods

Patients

The study was carried out in 106 subjects preselected at outpatient clinics on the basis of the following criteria: they had mild-to-moderate essential hypertension, never treated or untreated for at least 2 weeks, with no clinical evidence of congestive heart failure, coronary disease, renal insufficiency or any other occlusive artery disease. They were 69 men and 37 women aged 20–72 years. Patients were recalled to have an ambulatory blood pressure monitor fitted, between 0830 and 1000 h. After a normal day's activity, patients returned to the hospital at 0800 h the following morning, whereupon the monitor was removed and a full aetiological and cardiovascular risk factor examination was performed in the outpatient clinic [12]. Patients with known plasma glucose or lipid abnormalities and subjects with body mass index > 30 kg/m^2 were not included.

Methods

Casual blood pressure measurements

Blood pressures and heart rates were measured by highly qualified practitioners on three occasions: at the preselection visit, before the ambulatory blood pressure monitor had been fitted and when the device was returned to the hospital. Measurements were performed in triplicate at 1 min intervals after the patient had rested for 10 min in the supine position and in duplicate after the patient had stood for 2 min, using a mercury sphygmomanometer with an appropriate cuff circumference. Systolic blood pressure was determined by Korotkoff phase I and diastolic blood pressure by phase V. The means of the triplicate supine blood pressure values recorded before fitting the monitor were used in the statistical analysis.

Non-invasive ambulatory blood pressure monitoring

Automated non-invasive blood pressure monitoring was carried out in each patient using a DIASYS model 200RS monitor (Novacor, Rueil-Malmaison, France) programmed to measure blood pressure and heart rate every 15 min throughout 24 h. The reliability of this method has previously been evaluated versus that of the intra-arterial method [13]. Ambulatory monitoring was undertaken for a full active day; the patient worked normally during the day and then went home as usual in the evening [14]. The data of each full day's recording were averaged over the hourly periods, the 24 h period, daytime (0700–2200 h) and night-time (2200–0700 h); these mean values were used for the statistical analysis. Circadian variability was assessed on the basis of individual SD and nocturnal falls were evaluated from individual data of each subject.

Arterial distensibility

The pressure pulse generated by ventricular ejection is propagated throughout the arterial tree at a speed determined by the elastic and geometrical properties of the arterial wall and the blood density. Since fluid is contained in a system of elastic conduits, energy propagation occurs predominantly along the arterial wall [15]. The thickness of the arterial wall and the lumen diameter thus become the major determinants of pulse-wave velocity (PWV). This concept has been formalized in a mathematical model [16], whereby the pulse-wave velocity is given by the Moens–Korteweg equation: $PWV = \sqrt{Eh/(2\rho R)}$, or by the Bramwell–Hill equation: $PWV = \sqrt{\Delta P\, V/(\Delta V \rho)}$, where E is Young's modulus of the arterial wall, h is the wall thickness, R is the arterial radius, ρ is the blood density and ΔV and ΔP are, respectively, the changes in volume and in arterial pressure.

The pulse-wave velocity is calculated from measurements of the pulse transit time and the distance travelled by the pulse between two recording sites: PWV = distance/transit time (m/s) [17]. The pulse wave was recorded using a TY-306 pressure-sensitive transducer (Fukuda, Tokyo, Japan).

Automatic measurements of pulse-wave velocity

For automatic measurements of pulse-wave velocity, we used the automatic device Complior (COLSON, Garges les Gonesse, France) [18]. Briefly, the pressure waveforms are digitized at 500 Hz frequency acquisition for carotid–femoral artery PWV. The two pressure waveforms are stored in a memory buffer. A preprocessor analyses automatically the gain of each waveform and adjusts it to provide equality of the two signals. When the operator observes a pulse waveform of sufficient quality on the computer screen, digitization is suspended and calculation of the time delay between the two pressure upstrokes is initiated. The first operation performed is to remove spikes that may be present in the pulse waveforms, which are then digitally differentiated and the times at which peak values occur are determined. The delay between the two pulse waves is calculated by performing a correlation between the data of the two waveforms. The distal pressure upstroke is then time-shifted by subtracting one sample period and the correlation coefficient is again calculated. The procedure is repeated until the amount of data point shift required to provide the best fit has been calculated. This procedure was repeated for 10 different cardiac cycles and their mean value was considered for the analysis. Validation of this method has previously been described [18] by comparison with the standard method. The mean difference value was 0.20 ± 0.45 m/s; its intra-observer and interobserver repeatibility coefficients were, respectively, 0.935 and 0.890.

Statistical analysis

Data were transferred to a spreadsheet software, Excel 5.0 (Microsoft Co., Washington DC, USA), for analysis on

a personal computer. The quality of the data acquisition was double-checked by two different observers before data were transferred to the statistical software, Systat (Systat for Windows 5.1, Evanson, Illinois, USA). Descriptive tests were used to express the range values. Comparison of mean values between groups was performed using an unpaired Student's t-test. Comparison of qualitative parameters was performed using the χ^2-test. Simple regression analysis was performed by calculating Pearson's correlation coefficient. Stepwise analysis was used for multiple regression. Values are expressed as means ± SD. $P < 0.05$ was considered statistically significant.

Results

Patients

One hundred and six patients (69 men, 37 women) participated in the study. On the basis of the casual blood pressure measurements, 21 subjects were normotensives and 85 presented essential hypertension. Their characteristics (mean ± SD) were age 49 ± 11 years, for body mass index 25.1 ± 3.0 kg/m^2, pulse-wave velocity 11.82 ± 3.1 m/s, total plasma cholesterol 5.56 ± 0.96 mmol/l and 5.43 ± 0.92 mmol/l for plasma glucose.

Table 1 shows the different mean values of blood pressure and heart rate obtained from the casual and ambulatory measurements. For the latter, results are expressed separately for the full 24 h, the daytime and the nighttime periods. The night fall is expressed as a percentage of the day values: day – night/day × 100.

Table 1 Mean values of blood pressure and heart rate

	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Heart rate (beats/min)
Casual measurements	161 ± 18	102 ± 12	72 ± 8
24 H	143 ± 16	92 ± 11	74 ± 11
Daytime (0700–2200 h)	149 ± 16	97 ± 11	78 ± 12
Night-time (2200–0700 h)	131 ± 17	82 ± 12	66 ± 11
Night fall (%) (day – night/day)	13.4 ± 8.0	16.2 ± 7.9	12.6 ± 6.0

Values are expressed as means ± SD.

Table 2 Comparison of blood pressure and heart rate profile in patients with low (below the median) and high (above the median) pulse-wave velocity values

	Low pulse-wave velocity (below the median value)	High pulse-wave velocity (above the median value)
Men/women	21/32	16/37
Normotensives/hypertensives	14/39	7/46
Age(years)	44 ± 9	53 ± 9***
Body mass index (kg/m^2)	24.9 ± 2.6	25 ± 2.4
Pulse-wave velocity (m/s)	9.52 ± 0.98	14.00 ± 1.96***
Casual SBP (mmHg)	158 ± 14	164 ± 14*
Casual DBP (mmHg)	101 ± 10	103 ± 9
Casual heart rate (beats/min)	72 ± 8	75 ± 12
24 H SBP (mmHg)	139 ± 11	147 ± 12**
24 H DBP (mmHg)	89 ± 8	94 ± 8*
24 H heart rate (beats/min)	71 ± 8	76 ± 8**
Day SBP (mmHg)	145 ± 12	153 ± 13**
Day DBP (mmHg)	95 ± 9	99 ± 8*
Day heart rate (beats/min)	75 ± 8	81 ± 9**
Night SBP (mmHg)	126 ± 12	137 ± 13***
Night DBP (mmHg)	78 ± 9	85 ± 8***
Night heart rate (beats/min)	63 ± 8	69 ± 8***
SBP night fall (%)	15.6 ± 7.4	12 ± 4.4**
DBP night fall (%)	18.4 ± 7.6	14 ± 4.7**
Heart rate night fall (%)	12 ± 5.8	13.5 ± 6.2

Values are expressed as means ± SD. DBP, diastolic blood pressure; SBP, systolic blood pressurse. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$, versus low pulse-wave velocity.

Relationship between arterial distensibility and clinical parameters

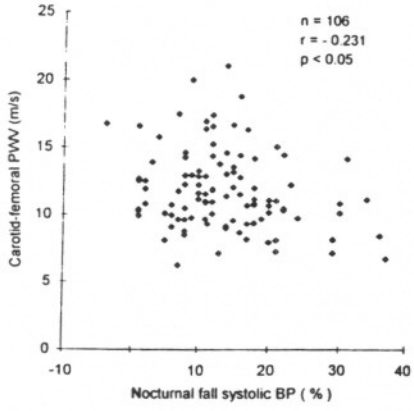
Analysis based on simple linear correlation showed that pulse-wave velocity is highly correlated to age (r = 0.447, $P < 0.001$) and, to a lesser extent, to blood pressure and heart rate. With regard to blood pressure, pulse-wave velocity is correlated mostly to systolic blood pressure (SBP) both for the casual (r = 0.254, $P < 0.01$) and for the 24 h ambulatory measurements (r = 0.257, $P < 0.01$); for the latter method, the highest correlation coefficient is observed with the nocturnal period values (r = 0.305, $P < 0.01$) in comparison with the diurnal period (r = 0.245, $P < 0.05$). Concerning the diastolic blood pressure (DBP), a significant correlation is observed only with the ambulatory measurements during the nocturnal period (r = 0.24, $P < 0.05$). For heart rate, only the ambulatory values were significantly correlated to pulse-wave velocity, with the 24 h period (r = 0.191, $P < 0.05$) and mainly with the nighttime period (r = 0.24, $P < 0.05$).

On this basis, a multiple regression analysis was performed, between pulse-wave velocity (as dependent variable) and age, mean 24 h SBP and heart rate (as independent variables). Stepwise multiple regression analysis showed that age is the strongest predictor of pulse-wave velocity (standard coefficient 0.432, $P < 0.001$), followed by mean 24 h heart rate (standard coefficient 0.183, $P = 0.04$). Mean 24 h SBP showed a positive trend that did not attain statistical significance (standard coefficient 0.154, $P = 0.08$).

Analysis according to the arterial distensibility values

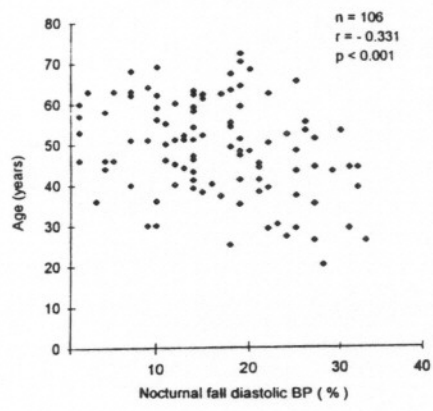
According to the median value of pulse-wave velocity (median 11.1 m/s), patients were classified into two groups: high pulse-wave velocity (above the median) and low pulse-wave velocity (below the median). No difference was noted in the sex distribution or in the prevalence of essential hypertension between the two defined groups (Table 2). Patients with high pulse-wave velocities were significantly older and presented blood pressure and heart rate levels higher than those found in subjects with low pulse-wave velocities. These differences were more pronounced in the ambulatory data,

Fig. 1



Correlation between nocturnal fall in systolic blood pressure (BP) and carotid–femoral artery pulse-wave velocity (PWV).

Fig. 2



Correlation between nocturnal fall in diastolic blood pressure (BP) and age.

mainly for the nocturnal period, than they were the casual measurement values. With regard to the circadian variability, no difference was found in the SD of the SBP or the DBP, whereas significantly lower falls both in SBP and in DBP during the night period were noted in subjects with high pulse-wave velocities. No significant difference was found between the nocturnal changes in heart rate in the two groups. The results are summarized in Table 2.

Night falls in blood pressure and heart rate

To gain further insight, a univariate regression analysis was performed comparing the percentage falls in the blood pressure values during the night with those during the daytime period (ΔSBP and ΔDBP). ΔSBP presented a significant negative correlation with mean 24 h SBP ($r = -0.198$, $P < 0.05$) and with pulse-wave velocity ($r = -0.231$, $P < 0.02$). ΔDBP showed a significant negative correlation with age ($r = -0.331$, $P < 0.001$), pulse-wave velocity ($r = -0.224$, $P < 0.02$) and mean 24 h blood pressures (SBP: $r = -0.211$, $P < 0.05$; DBP: $r = -0.195$, $P < 0.05$). The multiple stepwise regression analysis showed that only pulse-wave velocity was a predictor for ΔSBP (multiple $R = -0.272$, $P < 0.02$; Fig. 1), whereas age (multiple $R = -0.340$, $P < 0.01$) and, to a lesser extent, mean 24 hour DBP (multiple $R = -0.195$, $P < 0.05$) were independent predictors for ΔDBP (Fig. 2).

Discussion

Several clinical studies [19–22] have emphasized that age and blood pressure are the most important factors contributing to increase pulse-wave velocity. In fact, since the arterial wall elastic modulus is a function of intra-arterial pressure and the pulse-wave velocity is related to wall elasticity, the pulse-wave velocity is related directly to distending pressure [22]. On the other hand, age is an important factor contributing to the increase in pulse-wave velocity because of increased arterial stiffness, medial calcification and loss of elasticity with age [23]. Considering these observations, the major findings of the present study are the following: pulse-wave velocity is correlated significantly with heart rate; subjects with reduced arterial distensibility present higher blood pressure and heart rate values recorded by the ambulatory blood pressure monitoring, mainly during the night period with reduced nocturnal falls both in SBP and in DBP; and pulse-wave velocity appears to be an independent predictor of the nocturnal fall in SBP.

Relationship between pulse-wave velocity and heart rate

The finding of a correlation between heart rate and pulse-wave velocity seems remarkable since it remained significant when analysed by multiple regression. In addition, patients with high pulse-wave velocities present constantly higher heart rate values than do patients with low pulse-wave velocities. Such a relationship between pulse-wave velocity and heart rate was noted in previous studies [11,12]. In fact, because the viscous component of the elastic arterial wall is known to be highly frequency-dependent, it is expected that the higher values of heart rates might be associated with the more reduced distensibility [24–27]. Thus, for a given value of blood pressure, arterial stiffness is expected to be higher when the heart rate is increased. This frequency-dependence of the various indices of arterial stiffness becomes a particularly important quantity to evaluate in human populations because numerous epidemiological reports [28,29] *in vitro* and experimental studies [30,31] have emphasized that an elevated heart rate is associated with an increased occurrence of cardiovascular injuries and events.

Considering the observation of a correlation between heart rate and arterial distensibility and the results observed for SBP and heart rate mainly during night-time, it is important to consider the possible role of the autonomic nervous system. In fact, the activation of this system is usually associated with an increase in heart rate and a decrease in the arterial distension capacity. Moreover, the autonomic system is involved in the baroreceptor sensitivity regulation, which is usually evaluated by analysis of the relationship between SBP and heart rate period [32]. Since several reports associated circadian changes in cardiovascular haemodynamics with an increase in baroreceptor sensitivity during sleep [33–36], and hypertension is associated with an impairment of baroreflex regulation, it seems logical that this abnormality appears mainly when the baroreceptor is highly sensitive, such as during the night, and affects SBP and heart rate, two parameters that are involved in the assessment of baroreceptor sensitivity. Finally, several reports [37,38] showed an association between some abnormalities of the autonomic nervous system and disturbances in the circadian rhythm of blood pressure noted, as in our study, mainly during the night-time.

Arterial distensibility and blood pressure circadian variability

In this study, there was no significant difference between the SD calculated individually for SBP and DBP in patients with high and in those with low pulse-wave velocity values. Since SD may be considered to reflect the 'short-term variability' of blood pressure [39], we may argue that pulse-wave velocity does not affect short-term blood pressure variability evaluated by intermittent non-invasive monitoring significantly in this population.

The pattern is quite different when we analyse the circadian rhythm, namely, the day–night variability. Subjects with high pulse-wave velocities present, in comparison with those with low pulse-wave velocity values, about a 5% increase in the mean diurnal blood pressure values (both for SBP and for DBP) and about a 9% increase in the mean nocturnal values. This difference could not be accounted for by dipper status (arbitrarily defined as a fall of more than 10% both in SBP and in DBP during night-time), since the prevalence of dippers was similar in the two groups (n = 36, 66.6%, in patients with low pulse-wave velocities versus n = 31, 58.5%, in patients with high pulse-wave velocities).

It has previously been reported [40] that day–night changes in arterial distensibility are correlated to day–night changes in blood pressure; in this study, a negative correlation was noted between pulse-wave velocity and the fall in nocturnal blood pressure, both for SBP and for DBP. It is difficult to know whether a change in pulse-wave velocity is causing the increase in nocturnal blood pressure or vice versa. On the multivariate analysis, pulse-wave velocity appears as an independent predictor of the nocturnal fall in SBP; this may be explained by the observation that an increased pulse-wave velocity is associated with an increase in SBP [41] and thus a reduced nocturnal fall may be expected in these patients, mainly in the SBP values, as has been described in patients with arterial diseases [42]. However, the independent predictors of the nocturnal fall in DBP were age and mean 24 h blood pressure level, two well-known parameters described previously in several reports [43,44].

Conclusion

The present study showed that the reduction in aortic distensibility evaluated by carotid–femoral artery pulse-wave velocity is associated with increased blood pressure and heart rate levels and disturbances of the circadian blood pressure profile with increased nocturnal values. It also showed that arterial distensibility appears to be an independent predictor of the nocturnal fall in SBP. Since there is an increased risk of organ damage and vascular events in the presence of higher nocturnal blood pressure values, and since the circadian profile of blood pressure levels should influence the dosage and the time interval between antihypertensive drug administrations, our findings suggest that a study of arterial distensibility in the normal follow-up of hypertensive patients might be of benefit.

Acknowledgements

The authors thank Mrs Z. Khalil for her statistical assistance and analysis, Miss Ch. Kaikati for her technical assistance and Mrs S. Daubanes for her secretarial assistance.

References

1 Dorhurst AC, Howard P, Leathart GL: **Respiratory variations in blood pressure.** *Circulation* 1952, **6**:553–558.

2 Shimada SG, Marsh DJ: **Oscillations in mean arterial blood pressure in conscious dog.** *Circ Res* 1979, **44**:692–700.

3 Littler WA, Honour AJ, Carter RD, Sleight P: **Sleep and blood pressure.** *BMJ* 1975, **3**:346–348.

4 O'Brien E, Sheridan J, O'Malley K: **Dippers and non-dippers [letter].** *Lancet* 1988, **ii**:397.

5 Baumgart P, Walger P, Dorst KG, von Eiff M, Rahn KH, Vetter H: **Can secondary hypertension be identified by 24h ambulatory monitoring?** *J Hypertens* 1989, **7 (suppl 3)**:S25–S28.

6 Fagard R, Staessen JA, Thijs L: **The relationships between left ventricular mass and daytime and night-time blood pressures: a meta-analysis of comparative studies.** *J Hypertens* 1995, 13:823–829.

7 Shimada K, Kawamoto A, Matsubayashi K, Nishinaga M, Kimura S, Ozawa T: **Diurnal blood pressure variations and silent cerebrovascular damage in elderly patients with hypertension.** *J Hypertens* 1992, **10**:875–878.

8 Verdecchia P, Schillaci G, Gatteschi C, Zampi I, Battistelli M, Bartoccini C, *et al.*: **Blunted nocturnal fall in blood pressure in hypertensive women with future cardiovascular morbid events.** *Circulation* 1993, **88**:986–992.

9 Safar ME, Simon Ach: **Hemodynamics in systolic hypertension.** In *Handbook of Hypertension, Volume 7: Pathophysiology of Hypertension. Cardiovascular Aspects.* Edited by Zanchetti A, Tarazi RC. Amsterdam: Elsevier Science; 1986:225–241.

10 Asmar R, Pannier B, Santoni JP, Levy B, Safar M: **Reversion of cardiac hypertrophy and arterial compliance after converting enzyme inhibition in essential hypertension.** *Circulation* 1988, **78**:941–950.

11 Asmar RG, Brunel PC, Pannier BM, Lacolley PJ, Safar ME: **Arterial distensibility and ambulatory blood pressure monitoring in essential hypertension.** *Am J Cardiol* 1988, **61**:1066–1070.

12 Cunha RS, Benetos A, Laurent S, Safar M, Asmar RG: **Distension capacity of the carotid artery and ambulatory blood pressure monitoring. Effects of age and hypertension.** *Am J Hypertens* 1995, **8**:343–352.

13 Barthelemy JC, Geyssant A, Auboyer C, Antoniadis A, Berruyer J, Lacour JR: **Accuracy of ambulatory blood pressure determination: a comparative study.** *Scand J Clin Lab Invest* 1991, **51**:461–466.

14 Asmar RG, Girerd XJ, Brahimi M, Safavian A, Safar ME: **Ambulatory blood pressure measurements, smoking and abnormalities of glucose and lipid metabolism in essential** hypertension. *J Hypertens* 1992, **10**:181–187.

15 Avolio AP: *Pulse Wave Velocity and Hypertension in Arterial and Venous Systems in Essential Hypertension.* Edited by Safar M. Boston: Martinus Nijhoff; 1991:133–152.

16 Bramwell JC, Hill AV, McSwiney BA: **The velocity of the pulse wave** in **man in relation to age as measured by the hot-wire sphygmograph.** *Heart* 1923, **10**:233–255.

17 Avolio AP, Fa-Quan D, Wei-Qiang L, Yao-Fei L, Zhen-Dong H, Lian-Fen XL, *et al.*: **Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China.** *Circulation* 1985, **71**:202–210.

18 Asmar R, Benetos A, Topouchian J, Laurent P, Pannier B, Brisac AM, *et al.*: **Assessment of arterial distensibility by automatic measurements of pulse wave velocity.** *Hypertension* 1995, **26**:485–490.

19 Avolio AP, Chen S, Wang R, Li M, O'Rourke MF: **Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community.** *Circulation* 1983, **68**:50–58.

20 Eliakim M, Sapoznikov D, Meinman J: **Pulse wave velocity in healthy subjects and in patients with various disease states.** *Am Heart J* 1971, **82**:448–457.

21 Schimmler W: **Untersuchungen zu Elastizitätproblemen der Aorta.** *Arch Kreislaufforschung* 1965, **47**:189–233.

22 Asmar R, Benetos A, London G, Hugue C, Weiss Y, Topouchian J, *et al.*: **Aortic distensibility in normotensive, untreated and treated hypertensive patients .** *Blood Pressure* 1995, **4**:48–54.

23 Learoyd MB, Taylor MG: **Alterations with age in the viscoelastic properties of human artery wall properties.** *Circ Res* 1966, **18**:278–292.

24 Bergel DH: **The dynamic elastic properties of the arterial wall.** *J Physiol* 1961, **156**:458–469.

25 Leung Y, Glagov S, Matthiews M: **Cyclic stretching stimulates synthesis of matrix components by arterial smooth muscle cells *in vitro*.** *Science* 1976, **191**:475–477

26 Glagov B, Zarins CK: **Retarding effects of lowered heart rate on coronary atherosclerosis.** *Science* 1984, **226**:180–182.

27 Nichols WW, O'Rourke MF: *McDonald's Blood Flow in Arteries: Theoretical Experimental and Clinical Principles.* Third Edition. London: Edward Arnold; 1990:77–196.

28 Dyer AR, Persky V, Stamler J, Paul O, Shekelle RB, Berkson DM, *et al.*: **Heart rate as a prognosis factor for coronary heart disease and mortality: findings in three Chicago epidemiological studies.** *Am J Epidemiol* 1980, **112**:736–749.

29 Kannel W, Kannel C, Paffenbarger R, Cupples LA: **Heart rate and cardiovascular mortality: The Framingham Study.** *Am Heart J* 1987, **113**:1489–1494.

30 Beere PA, Glagov S, Zarins CK: **Experimental atherosclerosis at the carotid bifurcation of the cynomolgus monkey.** *Arterioscler Thromb* 1992, **12**:1245–1253.

31 Manuck SB, Kaplan JR, Clarkson TB: **Behaviorally induced heart rate activity and atherosclerosis in cynomolgus monkeys.** *Psychosom Med* 1983, **56**:27–37.

32 Gribbin B, Pickering JG, Sleight P, Peta R: **The effect of age and blood pressure on baroreflex sensitivity in man.** *Circ Res* 1971, **29**:424–431.

33 DeLeeuw PW, Gaillard CA: **Circadian changes in the circulation.** *High Blood Pressure* 1992, **1**:245–247.

34 Floras JS, Hassan MO, Jones JV, Osikowska BA, Sever PS, Sleight P: **Consequences of impaired arterial baroreflexes in essential hypertension: effects on pressor responses, plasma noradrenaline and blood pressure variability.** *J Hypertens* 1988, **6**:525–535.

35 Parati G, Di Rienzo M, Bertinieri G, Pomidossi G, Casadei R, Groppelli A, *et al.*: **Evaluation of the baroceptor–heart rate reflex by 24-h intra-arterial blood pressure monitoring in humans.** *Hypertension* 1988, **12**:214–222.

36 Conway J, Boon N, Vann Jones J, Sleight P: **Involvement of the baroreceptor reflexes in the changes in blood pressure with sleep and mental arousal.** *Hypertension* 1983, **5**:746–748.

37 Ikeda T, Matsubara T, Sato Y, Sakamoto N: **Circadian blood pressure variation in diabetic patients with autonomic neuropathy.** *J Hypertens* 1993, **11**:581–587.

38 Imai Y, Abe K, Munakata M, Sakuma H, Hashimoto J, Imai K, *et al.*: **Circadian blood pressure variations under different pathophysiological conditions.** *J Hypertens* 1990, **8 (suppl 7)**:125S–132S.

39 Mancia G, Ferrari A, Gregorini L, Parati G, Pomidossi G, Bertinieri G, *et al.*: **Blood pressure and heart rate variability in normotensive and hypertensive human beings.** *Circ Res* 1983, **53**:96–104.

40 Kool MJF, Struijker-Boudier HA, Wijnen JA, Hoeks APG, van Bortel LM: **Effects of diurnal variability and exercise training on properties of large arteries.** *J Hypertens* 1992, **10 (suppl 6)**:S49–S52.

41 Nichols WW, O'Rourke MF, Avolio AP, Yaginuma T, Murgo JP, Pepine JC, *et al.*: **Effect of age in ventricular–vascular coupling.** *Am J Cardiol* 1985, **55**:1179–1184.

42 Asmar RG, Julia PL, Mascarel VL, Fabiani JN, Benetos A, Safar ME: **Ambulatory blood pressure profile after carotid endoarterectomy in patients with ischaemic arterial disease.** *J Hypertens* 1994, **12**:697–702.

43 Otsuka A, Mikami H, Nakamoto Y, Katahira K, Tsunetoshi T, Ogihara T: **Normal blood pressure recordings of elderly hypertensive patients at night.** *J Vasc Med Biol* 1990, **6**:306–309.

44 Coca A: **Circadian rhythm and blood pressure control: physiological and pathophysiological factors.** *J Hypertens* 1994, **12 (suppl 5)**:13S–21S.