Daily Life Blood Pressure Changes Are Steeper in Hypertensive Than in Normotensive Subjects

Giuseppe Mancia, Gianfranco Parati, Paolo Castiglioni, Roberto Tordi, Elena Tortorici, Fabio Glavina, Marco Di Rienzo

Abstract—Target organ damage in hypertensive patients is related to their increased average blood pressure and greater 24-hour blood pressure variability. Whether the rate of blood pressure changes is also greater in hypertension, producing a greater stress on arterial walls, is not known, however. Our study aimed at addressing this issue by computer analysis of 24-hour ambulatory intra-arterial blood pressure recordings in 34 subjects (29 males), 13 normotensive subjects and 21 uncomplicated hypertensive subjects (mean age±SD, 40.4±11.8 years). The number, slope (mm Hg/s), and length (beats) of systolic blood pressure ramps of 3 or more consecutive beats characterized by a progressive increase (+) or reduction (−) in systolic blood pressure of at least 1 mm Hg per beat were computed for each hour and for the whole 24-hour period. Twenty-four-hour average systolic blood pressure was 112.9±2.1 and 159.4±5.7 mm Hg in normotensive and hypertensive subjects, respectively. Over the 24 hours, the number and length of systolic blood pressure ramps were similar in both groups, whereas the slope was markedly different (24-hour mean±SE slope, 4.80±0.30 in normotensives and 6.50±0.40 mm Hg/s in hypertensives, P<0.05). Ramp slope was not influenced by age or reflex pulse interval changes, but it was greater for higher ramp initial systolic blood pressure values. Thus, in daily life, hypertensive subjects are characterized by steeper blood pressure changes than normotensives, and this, regardless of the mechanisms, may have clinical implications, because it may be associated with greater traumatic effect on the vessel walls of hypertensive patients. (Hypertension. 2003;42:277-282.)

Key Words: blood pressure ■ hypertension, arterial ■ baroreflex ■ blood pressure monitoring ■ autonomic nervous system

Epidemiological studies and antihypertensive drug trials have shown that systolic and diastolic blood pressure bear a clearcut relationship to the incidence of cardiovascular morbidity and mortality,1,2 which, for this reason, is greater in hypertensive than in normotensive individuals. Additionally, our group and others have shown (1) that this relationship is closer when 24-hour average blood pressures rather than office blood pressures are considered3–9 and (2) that, for any given 24-hour average blood pressure, the organ damage accompanying hypertension is more pronounced if the blood pressure variability that occurs over the 24 hours is greater.3–5,10,11–17 This evidence may suggest that a patient’s prognosis depends not only on average blood pressure level but, to some extent, also on the degree of daily life blood pressure fluctuation.

A third blood pressure phenomenon that may potentially affect organ damage and prognosis is the rate at which the changes in blood pressure over the 24 hours take place. This is because faster blood pressure changes may produce a greater stress on the arterial wall and thus more easily initiate the cascade of events that ultimately result in permanent cardiovascular lesions.18–21 The prevailing rate of blood pressure transient changes over the day and night in humans has never been investigated, however. Nor has any investigation determined whether this rate is similar or different in subjects with normal blood pressure compared with those with high blood pressure. Our study set out to address these 2 issues.

Methods

Subjects

Our study included a total of 34 nonsmoking subjects (29 males), whose body mass index ranged between 21 and 27 (mean±SE, 24.8±2.3). Occurrence of obstructive sleep apnea syndrome was reasonably, although indirectly, excluded by interview of spouses on subjects’ sleep features and by the evidence of a normal nocturnal blood pressure and heart rate fall in all subjects.22,23 Fourteen subjects (age 32.6±3.5 years, mean±SE) were normotensive volunteers in whom office blood pressure was persistently <140/90 mm Hg over 3 sets of office measurements performed at 1 month intervals, and 20 subjects were essential hypertensive (office blood pressure, measured as above, persistently ≥140/90 mm Hg; age

Received December 18, 2002; first decision January 8, 2003; revision accepted June 23, 2003.
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Hypertension is available at http://www.hypertensionaha.org

DOI: 10.1161/01.HYP.0000084632.33942.5F
Blood Pressure Measurement

In all subjects blood pressure was measured intra-arterially and in ambulatory conditions over 24 hours (Oxford system), by means of a catheter percutaneously inserted into the brachial or radial artery of the nondominant arm, following performance of the Allen test to establish preservation of the hand circulation by the ulnar artery. The catheter (positioned in the artery after local anesthesia with 2% lidocaine) was connected by a rigid-walled plastic tube to a plexiglas box placed on the chest at the heart level. The box contained the blood pressure transducer, a perfusion unit consisting of a 40 mL heparinized saline solution, and a miniaturized battery-operated peristaltic pump aimed at keeping the catheter patent throughout the 24 hours. The beat-to-beat blood pressure signal was stored on a magnetic cassette recorder (Oxford Medilog, Oxford Instruments) for subsequent analysis. During the recording the subjects were free to move within the hospital area and to engage in the social activities of hospital inpatients (TV watching, playing cards, walking in the hospital garden, visits from relatives, etc). Further details on the blood pressure monitoring technique used in this study are published. All subjects enrolled in the study after a detailed explanation of its nature and purpose. The protocol of the study was approved by the ethical committees of our institutions.

Data Analysis

In each subject the blood pressure signal was converted from analog to digital with a 12-bit resolution at 165 Hz. Systolic blood pressure (SBP) values were derived from each heart beat. SBP time series were scanned to identify SBP ramps of 3 or more consecutive beats characterized, respectively, by a progressive increase or reduction in SBP of 1 mm Hg per beat, which were termed SBP+ and SBP−, respectively. The ramp slope was estimated by computing the slope of the regression line between the SBP values included in the ramp and time. The ramp length was estimated by the number of beats included in the ramp. SBP+ and SBP−, accompanied and unaccompanied by reflex changes in pulse interval (lengthening and shortening, respectively), were separately analyzed. Pulse interval was determined at parabolic interpolation of the pulse waveform peak. Previous studies have shown this to correspond to RR interval values obtained following local anesthesia with 2% lidocaine) was connected by a rigid-walled plastic tube to a plexiglas box placed on the chest at the heart level. The box contained the blood pressure transducer, a perfusion unit consisting of a 40 mL heparinized saline solution, and a miniaturized battery-operated peristaltic pump aimed at keeping the catheter patent throughout the 24 hours. The beat-to-beat blood pressure signal was stored on a magnetic cassette recorder (Oxford Medilog, Oxford Instruments) for subsequent analysis. During the recording the subjects were free to move within the hospital area and to engage in the social activities of hospital inpatients (TV watching, playing cards, walking in the hospital garden, visits from relatives, etc). Further details on the blood pressure monitoring technique used in this study are published. All subjects enrolled in the study after a detailed explanation of its nature and purpose. The protocol of the study was approved by the ethical committees of our institutions.

24h SBP (hourly means ± SE)

Figure 1. Hourly systolic blood pressure (SBP) and heart rate (HR) values in normotensive (N) and hypertensive (H) subjects. Data are shown as mean±SE.

Correction. The Pearson correlation coefficients were computed between ramp parameters and 24-hour average blood pressure values. Ramp parameters were also averaged over different tertiles of SBP measured at the beginning of the ramp. Given the age difference between groups, the potential influence of this factor in accounting for the differences in ramp parameters between normotensive and hypertensive subjects was addressed by linear correlation analysis between ramp parameters and age. Statistical significance was determined at P<0.05. Unless otherwise stated, the symbol ± refers to the standard error of the mean. Statistical analysis was carried out by using SPSS software (SPSS Inc).

Results

The 24-hour average SBP was 112.9±2.1 mm Hg in the normotensive and 159.4±5.7 mm Hg in the hypertensive group, with a typical circadian blood pressure profile in both groups (Figure 1).

As shown in Figure 2 (left panel), in both the normotensive and the hypertensive groups, there were hundreds SBP+ and SBP− ramps over the day and night, for a total of several thousand ramps of each type over the whole 24-hour recording period, the number of both types of ramps being somewhat less during the night than during the daytime. There was no significant difference in the number of the SBP+ and the SBP− ramps between normotensive and hypertensive subjects during the day, whereas either ramp type was significantly more frequent in the latter than in the former group during the night (Figure 2).
As shown in Figure 2 (central panel), the length of the SBP+ and SBP− ramps was (1) usually about 41/2 beats, (2) less during the night than during the day, and (3) superimposable over the 24 hours in normotensive and hypertensive subjects. This was not the case for the ramp slope, however, which throughout the 24 hours was invariably greater in hypertensive than in normotensive subjects (Figure 2, right panel, and Figure 3). For the whole 24-hour period, the difference amounted to +26.9% for SBP+ and +37.0% for SBP− ramps, in both instances reaching statistical significance. The difference in slope between the 2 groups showed no correlation with age (Figure 4) and remained statistically significant when the ramps unaccompanied by reflex changes in pulse interval were separately considered (Figure 5). When tertile SBP values at the beginning of the ramps were plotted versus the corresponding ramp slope values (SBP+ and SBP− pooled), there was a tendency for the ramp slope to be greater as the initial SBP was greater. This was the case both for the normotensive and for the hypertensive group (Figure 6).

Figure 2. Average 24-hour, daytime and nighttime values for the number, length, and slope of SBP ramps (ramps+ and ramps− pooled). Data are separately shown for normotensive (N) and hypertensive (H) subjects. Asterisks refer to the level of statistical significance of the between-group differences.

Figure 3. Hourly slope of SBP ramps in normotensive (●) and hypertensive (○) subjects. Data (mean±SE) are shown separately for SBP+ and SBP− and for the ramps of either type pooled.

Figure 4. Relationship of ramp slope (lower panel) and ramp number (upper panel) with age in all the normotensive and the hypertensive subjects of our study.
The mechanisms responsible for the greater steepness of the SBP changes seen in hypertensive patients are not clarified by our study. It should be emphasized, however, that in spite of the age difference between the 2 groups, this phenomenon was not due to aging per se, because in the total population of the study subjects, age did not bear any relationship with ramp slope. It should also be emphasized that the greater steepness of the SBP changes in hypertensive patients did not depend on the reduced ability of these subjects to oppose fast-occurring blood pressure alterations through baroreflex changes in heart rate,29 because the difference in ramp slope between the hypertensive and the normotensive group persisted when only SBP ramps unaccompanied by reflex heart rate modifications were analyzed. Thus, other possibilities should be considered. One, the steeper changes in SBP observed in hypertensive subjects could be due to the fact that the blood pressure effect of environmental and psychological stimuli typical of daily life were magnified at the vascular level by the increased wall stiffness and/or the greater wall-to-lumen ratio30 that characterizes hypertension. An additional possibility is that the SBP changes were steeper in hypertensive patients because, in these patients, the blood pressure effects of environmental and psychological stimuli are enhanced at a central level. This would imply that, as described for animal models of hypertension,31–33 human essential hypertension is also characterized by a sympathetic hyper-reactivity to a variety of daily life stimuli. A third possibility is that the steeper SBP changes seen in hypertensive patients are accounted for by the inverse relationship that exists between large artery distensibility and blood pressure.34–36 That is, as blood pressure increases, large arteries become stiffer, causing a greater SBP change for any given change in stroke volume. These possibilities are not mutually exclusive, and all may contribute to the differences we have found. The data reported in Figure 6, however, may score in favor of a major contribution of the last mechanism because, at a similar SBP (the highest tertile of the normotensive and the lowest tertile of the hypertensive group), the ramp slopes were similar in normotensive and hypertensive patients. This suggests that the higher slope of SBP ramps in hypertensive patients than in normotensive subjects may largely be due to their higher blood pressure levels per se.

Compared with the daytime, nighttime sleep is by and large characterized by a lower blood pressure level and a smaller blood pressure variability. Our study provides the first evidence that this condition is characterized also by blood pressure changes that are less steep than during the day, this being the case both in subjects with normal and in subjects with an elevated blood pressure. This may offer an additional explanation for the lower rate of cardiovascular morbidity and fatal events that have repeatedly been shown to occur during the night.37 That is, this lower rate may depend, among other nonmechanical factors,38 on a lower and more stable blood pressure. It may additionally depend, however, on the fact that blood pressure changes take place less steeply.

Finally, we would like to address a few potential limitations of our study. First, our analysis is based on data collected in 34 subjects. This might appear as a relatively small number. However, to maximize accuracy of slope estimations and make
the data relevant to daily life conditions, we had to use 24-hour intra-arterial blood pressure recordings, which prevented large numbers of patients from being involved. Furthermore, the amount of information obtained was not small if one considers that a beat-by-beat recording carried out for 24 hours allows a huge amount of data to be obtained for each individual subject (more than 104,000 pulse waves for each recording). Second, our study included mostly male subjects, which prevents us from evaluating possible gender differences in the phenomenon we have described. This issue will have to be addressed in future studies.

**Perspectives**

Our study adds novel information on the characteristics of BP variability at normal and high blood pressure, by providing for the first time data on the slope of beat-by-beat BP changes in humans, assessed in daily life conditions. Data collected by 24-hour ambulatory intra-arterial BP recordings clearly show that, in daily life, hypertensive patients are characterized by fast and short-duration SBP increases and reductions that are steeper than in normotensive subjects throughout the day and night. These steeper BP changes may result from sympathetic hyperreactivity to daily life stimuli, arteriolar remodeling, and/or greater arterial stiffness. Regardless of the mechanisms, the increased ramp steepness may have clinical implications, because steeper rises and falls in intravascular pressure may be associated with greater traumatic effect on the vessel walls and may facilitate vascular damage. This should nevertheless be further addressed by future investigations, possibly taking advantage of the present availability of noninvasive techniques for continuous blood pressure monitoring.39—41

**References**


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Hypertension. 2003;42:277-282; originally published online July 28, 2003; doi: 10.1161/01.HYP.0000084632.33942.5F

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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http://hyper.ahajournals.org/content/42/3/277

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