Nonsymmetrical double logistic analysis of ambulatory blood pressure recordings

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AMBULATORY BLOOD PRESSURE (ABP) monitoring devices are now very widely used for detecting white coat hypertension, for adjusting drug therapy for hypertensive patients, as well as for predicting the level of hypertension-induced enlargement of the heart and thickening of the blood vessels (10). ABP recorders have also confirmed earlier findings by invasive methods that there is a clear diurnal pattern in blood pressure (BP). Values are highest in the morning, decrease gradually during the day, and reach the lowest values at night. Although the exact mechanisms for the rhythm are not yet fully understood, physical activity and periods of rest strongly influence the diurnal BP pattern (7).

Known methods of analysis of circadian rhythms have generally involved averaging BP records at fixed clock times or synchronizing records relative to the time of waking. Thus the data are segmented into a higher pressure period, approximating the daytime awake period, and a low-pressure period corresponding to the nighttime sleep period. The difference in these two BP levels constitutes the major circadian variation in BP. However, this approach is rather limited, and a more robust method is desirable. The most common approach in this regard has been the Minnesota Cosinor method, which assumes that the high- and low-BP periods have the same length, that the diurnal pattern follows, in principle, a sine wave, and that the transition is smooth, symmetrical, and continuous (8, 13, 19). This method gives information about the phase and amplitude of oscillations, but it is not clear that circadian changes in BP and heart rate (HR) necessarily follow the slow and smooth changes suggested by a cosine function. An extension of this approach has been to apply a Fourier analysis, which constitutes the superposition of multiple cosine functions of different amplitude and frequency (2). A recent method has involved the application of a simple square-wave mathematical model that involves the estimation of the daytime and nighttime plateau with a vertical transition between the two periods, resulting in a square-wave pattern (5). Although this method has been shown to be better than the cosinor method, it assumes an abrupt and complete transition within one time point, which is clearly not the case in practice.

To date, there have been no methods that separately determine the rate of increase in BP and HR in the morning and the rate of decrease in the evening. Indeed, a considerable need has arisen to provide a robust method of analysis of circadian changes in cardiovascular parameters because it has become clear that the occurrence of strokes, cardiac infarcts, and subarachnoid hemorrhage is unevenly distributed over the day, with the highest incidence in the morning when BP is rising from low overnight values (22). Each of the known methods assumes a symmetrical pattern to a circadian rhythm.

The present study describes a novel method of analysis of circadian rhythm that provides a nonsymmetrical approximation curve representative of the circadian rhythm (4). This method has been applied to the circadian cardiovascular rhythms of normotensive and hypertensive rats and has re-

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revealed distinct asymmetric patterns (4). Importantly, we were able to show that hypertensive rats had a greater surge in arousal BP than normotensive rats. The new method involves combining an S-shaped logistic curve and its mirror image. This double logistic equation has a plateau with the day and night period, but the duration is not set and is determined by the individual response data. Importantly, there are two independent estimates of slope, one for evening and one corresponding to the changes in the early morning. Thus the method provides, for the first time, the ability to estimate the early morning increase in BP independently of the patterns or values obtained at other times of the day or night. We provide the first evidence that specific cardiovascular variables in humans follow a particular asymmetric diurnal pattern and that these differ between men and women.

**METHODS**

A total of 302 ABP data files were obtained at random and anonymously from a hypertension diagnostic referral clinic of the Alfred Hospital Medical Unit. A small number (3.3%) showed higher night blood pressures than day and were not included in further analysis. There were 140 men and 152 women aged on average 54.4 and 53.6 yr, respectively (range 21–88). They were generally referred to this clinic because they had been suspected of having borderline hypertension from the observations of clinic BP by local practitioners and were not on antihypertensive therapy. The study was approved by the Alfred Hospital Ethics Review Committee.

Cardiovascular measurements. ABP was recorded by use of a SpaceLabs 90207 or 90217 apparatus (SpaceLabs Medical, Redmond, WA). Monitors were set to measure every 30 min from late morning for 26 h during a typical day. In some early recordings, the monitors were set to hourly measurements during the night period. The first and last hour of the recordings were not included in the analysis because they involved fitting and removing the device in the clinic. An average of four data points per recording did not satisfy the criteria of the monitoring unit, and thus an average of 36.5 ± 0.6 data points were analyzed per recording (range 22–55). Diary recordings of awake and asleep times were available from 75 of the patients.

Analysis of mean arterial pressure-HR curves. ABP recordings were fitted to a six-parameter double logistic equation:

\[
\hat{y} = P_1 + \frac{P_2}{1 + e^{P_2/P_3 - x}} + \frac{P_2}{1 + e^{P_2/P_4 - x}}
\]

where \(P_1\) is the nighttime plateau, \(P_2\) is the difference between the day and night plateau, \(P_3\) is the rate of transition from day to night, \(P_5\) is the rate of transition between night and day, and \(P_4\) and \(P_6\) are the midtimes for these transitions. This equation is an extension of the four-parameter single logistic equation which has been used to fit dose response curves and baroreflex curves (16). The maximum slope of the curve during the transitions is \(P_2\times P_3/4\) for the transition from day to night and \(P_2\times P_5/4\) for the transition from night to day. The average slope is \(P_2\times P_3/4.562\) and \(P_2\times P_5/4.562\) (16), respectively. The data were fitted by a computer program written in LabVIEW that calculated the best estimate of each parameter (Fig. 1) using the least squares Marquardt algorithm (11). To automate the fitting procedure and minimize user intervention, a series of constraints were imposed on the parameters. In addition to the double logistic method, all data were processed by the Minnesota Cosinor and square-wave methods for comparison. Values were also determined according to clock times with 7 AM to 10 PM being day and 10 PM to 7 AM being considered night.

Details of the double logistic fitting procedure. The equation used to fit the ambulatory data was further extended to make it quasi-periodic, with four additional terms, related to changes in the preced-
DOouble Logistic Analysis of Ambulatory Recordings

Figure 2. Average double logistic fitted curves for SAP, MAP, DAP, and HR from male (solid lines, ○) and female (shaded lines, □) ambulatory recordings plotted over a 24-h period. Curves were reconstructed from the averages of the parameters of the double logistic equation. Error bars are SE. *P < 0.05 for the comparison between the day or night plateaus of men and women.

The four parameters P1, P2, P3, and P4 were checked with every full cycle of the algorithm to determine whether the constraints were met. If not, the parameter that regulates the fitting process of the Marquardt algorithm (λ) was increased. Thus when χ² became larger (as is the case in the normal iterative process), λ was increased 10-fold. If any of the parameter constraints were not satisfied, λ was increased 20-fold. In this way, the iterating process was never stopped when a constraint appeared. The search of minimal χ² value was simply restarted with another set of parameter values.

An example of the resulting double logistic curve of best fit for systolic arterial pressure (SAP), mean arterial pressure (MAP), diastolic arterial pressure (DAP), and HR from an individual patient is shown in Fig. 2. This figure illustrates the wide variation in the shape of the curve that can be accommodated by the double logistic equation.

Average values from the P1, P2, P4, and P6 were used to plot average group curves, whereas averaged log values of P3 and P5 were used to normalize the distribution.

Statistical analysis. Data are presented as means ± SE of the between-patient variation. Differences between curve parameters for men and women were compared by a Student’s t-test. For comparisons between the different fitting methods, we used a multifactor (method and group) repeated-measures ANOVA (1, 9). This is also called a split-unit or nested design, wherein the residual mean square for the between-group (male vs. female) comparisons contains the between-patient variance (patients × groups), whereas the within patient comparisons are based on a within patient variance estimate (i.e., the sum of the method × patient interaction from each group). Differences were considered significant when P < 0.05.

**RESULTS**

The 140 male and 152 female recordings showed a closely similar diurnal pattern of higher day and lower night BP and HR values (Fig. 2). Over the 24-h period DAP was slightly lower and HR slightly higher in women (P < 0.05, Table 1). The average BP values calculated at the day plateau by the logistic fitting procedure for systolic, DAP, MAP, and HR were 30–39% higher than the nighttime plateau levels in men and were similar in women (Fig. 2, Table 1, P < 0.001). There were relatively few gender differences in the day and night plateaus estimated by the double logistic method. HR was nearly 5% higher in women at night plateaus but not during the day (Table 1, Fig. 1, P < 0.05). There was no difference in the diurnal range between men and women (Table 1). Day and night averages estimated by fixed clock times underestimated both the day and the night plateau and the day-night difference by over twofold (Table 1). Clock-based calculations also

Table 1. Average results from the circadian analysis of 24-h blood pressure measurements from male and female patients analyzed by fixed clock times and also by the double logistic method

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Night</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>P</td>
</tr>
<tr>
<td><strong>Averages by clock</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP, mmHg</td>
<td>130.6 ± 1.07</td>
<td>127.8 ± 1.07</td>
<td>NS</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>95.7 ± 0.68</td>
<td>94.2 ± 0.75</td>
<td>NS</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>78.7 ± 0.63</td>
<td>76.4 ± 0.75</td>
<td>*</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>69.5 ± 0.90</td>
<td>72.0 ± 0.79</td>
<td>*</td>
</tr>
<tr>
<td><strong>Diurnal Range</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SAP, mmHg</td>
<td>33.4 ± 1.18</td>
<td>34.7 ± 1.20</td>
<td>NS</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>25.6 ± 0.96</td>
<td>26.8 ± 0.93</td>
<td>NS</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>24.5 ± 0.96</td>
<td>24.3 ± 0.74</td>
<td>NS</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>23.0 ± 0.99</td>
<td>22.6 ± 1.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Absolute values ± SE are shown in each column over the 24-h period. Significant difference between men and women: *P < 0.05, †P < 0.01. NS, not significant. SAP, systolic arterial pressure; MAP, mean arterial pressure; DAP, diastolic arterial pressure; HR, heart rate.

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showed larger differences between men and women, with the men having higher night levels of SAP, MAP, and DAP and lower HR than women (Table 1, P < 0.05). Both clock-based and logistic fitted estimates gave similar day values in men and women.

Dippers and nondippers. The prevalence of nocturnal “dipping” differed considerably depending on the method of analysis. A clock time definition based on <10% nighttime reduction from daytime MAP suggested that 32% of patients (n = 97) were nondippers. On the basis of diary values of awake and asleep times from 75 patients, 12 (16%) were defined as having <10% asleep reduction in MAP. The cosinor method showed that only 13% of patients were “nondippers” (n = 40), whereas the square-wave method detected 30 nondippers (10%). The double logistic method, however, showed that only 10 patients (3%, 6 male, 4 female) had a diurnal range of <10% of the day MAP plateau.

Circadian rates of change in cardiovascular variables. The average estimates of the six parameters estimated from the double logistic fitting procedure are shown in Table 2 for men and women. The P3 and P5 parameters reflect the steepness of the change from light to dark and dark to light, respectively, and a significant difference between them indicates “asymmetry.” Circadian BP patterns in men were symmetrical with similar rates of change from light to dark as to the rate from dark to light (Fig. 2, Table 2). By contrast, women showed an asymmetrical pattern with a more rapid reduction in MAP compared with the rate of morning rise in MAP (P < 0.05, Table 2, Fig. 2). A similar trend was observed with SAP and DAP, but these failed to reach significance. Women had also a much greater evening rate of reduction in MAP than men (P < 0.05) but a similar rate of reduction in DAP (Fig. 3). Interestingly, the rates of morning surge in BP were similar in men and women (Fig. 3).

The circadian pattern for HR showed an even greater degree of asymmetry, with 2.2- and 1.9-fold greater rate of morning increase in HR compared with the rate of evening decrease for men and women, respectively (Table 2, Fig. 2 and 3, P < 0.01).

Mid transition times and day-night durations. The double logistic equation parameters P4 and P6 reflect the middle of the transition time for the evening decrease and the morning increase in variables, respectively (Table 2). On average, the middle of the evening decrease occurred at 9:50 PM for BP and 8:50 PM for HR. Although women appear to decline earlier than men (Fig. 2), this was not statistically significant (0.6 ± 0.47 h for MAP). The middle of the morning increase in BP occurred at 8:10 AM and in HR at 9:20 AM, which was also similar in men and women (Table 2).

The durations of the light and dark periods (calculated time midway between light and dark plateaus) were 13.4 and 10.6 h, respectively, and were similar in men and women (calculated from P4 and P6 in Table 2).

In a proportion of patients (n = 75), the awake and asleep times were also recorded. For MAP, the time of going to sleep and the time of awaking were strong predictors of midpoint of the evening decrease and morning increase, respectively (P < 0.001, Fig. 4). By contrast, the awake and asleep times did not predict the diurnal range (Fig. 4).

Correlations with the rates of change in MAP. The rate of morning rise in MAP was associated with daytime MAP (r =

<table>
<thead>
<tr>
<th>Night Plateau</th>
<th>Range</th>
<th>Light to Dark</th>
<th>Dark to Light</th>
<th>Non symmetry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Rate P3</td>
<td>Slope P4</td>
<td>Transition time P5</td>
</tr>
<tr>
<td>SAP, mmHg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td>−1.60 ± 0.17</td>
<td>−10.78 ± 1.08</td>
<td>22.50 ± 0.32</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td></td>
<td>−1.42 ± 0.14</td>
<td>−7.14 ± 0.74</td>
<td>21.91 ± 0.30</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td></td>
<td>−1.48 ± 0.14</td>
<td>−7.09 ± 0.68</td>
<td>21.55 ± 0.28</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td></td>
<td>−0.87 ± 0.08</td>
<td>−3.81 ± 0.33</td>
<td>21.08 ± 0.35</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td>−0.99 ± 0.09</td>
<td>−4.15 ± 0.37</td>
<td>20.76 ± 0.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>−1.75 ± 0.17</td>
<td>−12.03 ± 1.16</td>
<td>21.97 ± 0.24</td>
</tr>
<tr>
<td></td>
<td></td>
<td>−1.92 ± 0.17</td>
<td>−10.29 ± 0.92</td>
<td>21.31 ± 0.21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>−1.71 ± 0.15</td>
<td>−8.31 ± 0.75</td>
<td>21.44 ± 0.23</td>
</tr>
<tr>
<td></td>
<td></td>
<td>−0.99 ± 0.12</td>
<td>−4.15 ± 0.37</td>
<td>20.76 ± 0.28</td>
</tr>
</tbody>
</table>

Values are means ± SE. P1, nighttime plateau; P2, range, calculated difference between night and day plateaus; P3 and P5, range-independent rates of change with units of h⁻¹. Nonasymmetry is based on the significance of the contrast between P3 and P5. *P < 0.05, †P < 0.001. Slope is the average rate of change in the parameter per hour.
0.21 for men and 0.22 for women, \( P < 0.01 \), Fig. 5) explaining \( \sim 5\% \) of the variance. The strongest predictor was a negative correlation with MAP range \( (r = 0.38 \text{ for men and } 0.35 \text{ for women}, P < 0.001) \), which explained \( \sim 14\% \) of the variance. There was also a correlation with nighttime MAP in men but not women. There was no correlation with age for either sex (Fig. 5).

The rate of evening fall in MAP was also related to the MAP range \( (r = 0.22 \text{ for men and } 0.29 \text{ for women}, P < 0.01) \), which explained \( \sim 5–9\% \) of the variance (data not shown). In women, the rate of fall was also weakly correlated with the night plateau, but not in men \( (r = 0.21, P < 0.05) \).

Reproducibility of the rate of change in BP. The coefficient of variation for the rate of morning rise in BP is quite high being 12 times higher than the 24-h BP plateau \( (10 \text{ vs. } 118\%) \). By contrast, the coefficient of variation for the day night difference is only four times \( (46\%) \). To examine the reproducibility of the rate of change in BP and HR, we compared values in 19 patients that had had two recordings on separate occasions \( (\text{average } 6.9 \text{ mo apart}) \). There was a strong correlation between the rate of morning rise on the first and second assessment for SAP \( (r = 0.513, P = 0.007) \), but not for HR \( (r = 0.1) \). On average, 26\% of the variability in this measure can be subtracted from the total when using a within-patient design. Furthermore, this finding suggests that a significant proportion of the variability is due to the patient and not to the technique itself.

Comparison of the double logistic, cosinor, and square-wave methods. The estimates of the maximum circadian variation by the three methods were compared. The double logistic method gave greater day-night differences for all parameters compared with either the cosinor or the square-wave method \( (P < 0.001, \text{ Table 3}) \).

The logistic method provided a better fit \( (56\%) \) than the square-wave \( (53\%, P < 0.001) \) or the cosinor method \( (41\%, P < 0.001) \) for BP (Fig. 6). A very similar trend was observed for HR \( (52, 49, \text{ and } 39\%, \text{ respectively, Fig. 6}) \).

**DISCUSSION**

We have used a new double logistic curve-fitting procedure to analyze ABP recordings of patients attending a hypertension assessment clinic. The double logistic method, developed originally for animal circadian analysis, makes relatively few assumptions about the shape of circadian variation of physiological measures and, being quite flexible, can readily accommodate quite a variety of patterns from square wave, sine wave to sawtooth, as well as all shapes in between (4). The main advantage of this method is that, as well as measuring the day and night plateaus, it can independently determine the positive and negative slopes of the transition between the plateaus. By comparing the slopes, a measure of symmetry or nonsymmetry can be made. It does not assume a continuous transition of data between a high and low peak value as does the cosinor method (19) or an abrupt transition as does the square-wave analysis (5). Inspection of 24-h data obtained from humans showed that transitions occur differently, in different parameters, in different groups and vary depending on whether it is an increase or decrease. The double logistic method is relatively simple, being essentially two dose response curves placed back to back. All six parameters have a biologically relevant meaning. P1 is the night plateau, P2 is the day-night difference, P3 and P5 represent the rate of transition between plateaus, and P4 and P6 represent the midpoint of the transition times. Thus the parameters are readily understandable and usable by most cardiovascular researchers.

The major findings of the present study are that there is evidence that in both men and women there is a marked asymmetry in the circadian HR pattern. The rate of morning rise in HR is very rapid compared with the rate of decline \( (2.1 \)
Interestingly, this is closely similar to what we observed in spontaneously hypertensive rats, in whom the arousal rate of increase in HR was 2.4 times the rate of decline \((4)\). By contrast, normotensive rats showed a symmetrical HR pattern. The underlying mechanisms at this stage are unclear, but the similarity of the pattern in hypertensive rats and humans suggests that it is probably not related to differences in human morning and evening behavioral patterns. In the animal studies there was no association of the asymmetric HR and locomotor activity patterns \((4)\).

The changing HR asymmetry patterns did not translate to rates of change in BP as might be produced if the HR reflected changes in cardiac output. Women showed an exaggerated rate of reduction in evening MAP compared with men and compared with the female rate of rise in BP. Men and women showed similar rates of rise in morning BP. Overall, men showed a BP symmetrical pattern. This may be extremely important because it means that overall 24-h MAP is lower in women because of a longer and earlier onset hypotensive phase. Thus our new method is able to assess the positive and negative circadian slopes quite independently, which is crucial to be able to further elucidate the mechanisms that occur during the transition from night to day and that underlie the male-female differences.

The mechanism underlying the more rapid reduction in evening MAP in women compared with men is a very interesting finding that may contribute to the well-known lesser incidence of cardiovascular events in premenopausal women \((3)\). Presumably there is a more rapid inhibition of the sympathetic nervous system, which is a major contributor to the nocturnal MAP reduction \((18)\). Interestingly, in men or women, there was no association with age of the rate of rise or fall in MAP and a separation of women into those less than 45 yr old and older than 55 showed virtually identical rates of rise.

**Table 3. Estimates of the maximum circadian variation (range) estimated by double-logistic, square-wave, and Cosinor curve fitting obtained from the analysis of 24-h data series of blood pressure and heart rate in men and women**

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th></th>
<th>Women</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Double Logistic</td>
<td>Square Wave</td>
<td>Cosinor</td>
<td>Double Logistic</td>
<td>Square Wave</td>
</tr>
<tr>
<td>SAP, mmHg</td>
<td>33.4±1.18</td>
<td>23.2±0.68†</td>
<td>27.3±1.08†</td>
<td>34.7±1.20</td>
<td>24.6±0.67†</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>25.6±0.96</td>
<td>17.4±0.52†</td>
<td>20.4±0.81†</td>
<td>26.8±0.93</td>
<td>19.2±0.51†</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>24.5±0.96</td>
<td>16.3±0.50†</td>
<td>19.5±0.77†</td>
<td>24.3±0.74</td>
<td>17.5±0.48†</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>23.0±1.0</td>
<td>15.0±0.5†</td>
<td>17.5±0.8†</td>
<td>22.6±1.1</td>
<td>14.6±0.5†</td>
</tr>
</tbody>
</table>

Values are means ± SE. Comparisons are between double logistic and the other methods as well as between men and women as determined by a multifactor (method and group) repeated-measures ANOVA \((1, 9)\). *\(P < 0.001\), men vs. women. †\(P < 0.001\), double logistic vs. square wave or cosinor.
and fall in MAP. Thus the mechanism is unlikely to be related to menopausal status. It also cannot be explained by a greater day-night difference, because this would have also affected the morning surge in MAP. At this stage, the mechanism is unclear and awaits further investigation.

It has been important to determine whether the rates of change in cardiovascular variables are independent variables or simply a reflection of other measures. The rates of change were relatively independent of the day or nighttime plateaus, with the former explaining <5% of the variance in rate. The best predictor was the day-night range, but the correlation was negative and accounted for 12–14% of the variance. This occurred even though the measure used for the correlation was the range-independent slope (units of h\(^{-1}\)) rather than the actual slope (units of mmHg/h). Removal of the constraint of P3 and P5 did not alter this relationship. This suggests that to a degree the small rises can occur more quickly, whereas those patients with very large day-night differences take longer to achieve them (Fig. 4). Importantly, we have provided evidence that the rate of change is a relatively reproducible measure within the same patient.

It is well known that physical state (awake or asleep) and levels of activity can influence the circadian cardiovascular pattern. In the present study, we have only made a very limited analysis of this aspect, which would clearly need more in-depth investigation. Nevertheless, we have established that there is a close correlation between the time of going to sleep and the time of blood pressure decrease in the evening. There was an even stronger correlation between the time of waking and the morning timing of the blood pressure increase. It is not surprising that these times are related as asleep-waking cycles (behavioral), and cardiovascular patterns become closely entrained via the influence of the suprachiasmatic nucleus (17). Furthermore, there is a close association between the reduction in cardiac baroreflex sensitivity in the morning and the surge in BP and HR as shown by 24-h monitoring in patients (14, 20). Surprisingly, the study by Nakazato and colleagues (12) suggests that the muscle sympathetic baroreflex gain goes down during sleep. However, they also observed that the gain remained suppressed after the subjects awoke. The combination of the reducing cardiac baroreflex gain and the remaining sympathetic baroreflex gain would be expected to make a considerable contribution to the surge in morning BP by lessening the normal baroreflex buffering capacity of the autonomic nervous system.

At this stage, the importance of the rate of rise in morning BP or HR as a risk factor is unknown. Recently, an important study by Karlo and colleagues (6) has shown that an excessive morning surge in BP is an independent risk factor for stroke in the elderly, independently of ABP, nocturnal BP falls, and silent infarct. After matching for age and 24-h BP, the top decile of patients with excessive morning surge in BP had a 2.7 times greater risk of stroke than the other group (low to normal morning surge in BP). Thus it has now been established that a high morning BP, even in treated patients, is an independent risk factor. Although this study used ambulatory recordings, only selected points of the 24-h data were used and no estimation of the rate of rise in BP was made.

All BP variables and HR showed a surprisingly similar degree of fit with the double logistic method, which was better than the square-wave fit and considerably better than cosinor fit. One of the other major differences was that double logistic method gave a better estimate of the day-night differences than either clock values, square-wave, or cosinor methods. Presumably, clock-based calculations as well as square-wave estimates contain values that are in the transition phase between plateaus. A major finding was that the various analysis methods produce quite different estimates of the number of nondippers. Fixed clock times estimated as many as one-third that failed to reduce MAP by 10% at night. Using patient recollections of being awake and asleep was better, detecting 16% as nondippers. The cosinor and square wave detected fewer patients, with the percentage of nondippers being 13 and 10%, respectively. However, these methods underestimated day-night differences owing to their constraints and poorer estimate of the diurnal pattern. The double logistic method gave the most accurate assessment of the day-night difference and detected only 3% nondippers. We observed similar numbers of men and female nondippers, which is consistent with previous studies (15). Because dipping status is considered a risk factor for cardiovascular disease (21), it is important for it to be accurately determined. Our analysis shows that large numbers of patients can be allocated to nondipping groups inappropriately owing to the definition being based on clock times or recollections of awake and asleep periods.

In conclusion, analysis of 24-h ambulatory recordings by a new logistic curve method reveals distinct asymmetric circadian patterns of cardiovascular and activity changes in male and female patients. The method detected a greater rate of decrease in MAP in women during the evening period compared with men that was not associated with differences in HR. The double logistic method provides better fitting of the data than is currently obtained by the square-wave or cosinor methods. The ability of this new analysis method to independently estimate the slopes of the changes between day and night plateaus may prove useful in future studies exploring the underlying mechanisms. Importantly, we have shown that this approach gives better estimates of the diurnal range in cardiovascular parameters and hence a more appropriate estimation of the proportion of nondippers.
REFERENCES