Reproducibility of Heart Rate Measured in the Clinic and With 24-hour Intermittent Recorders

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This study was undertaken to assess the reproducibility of office versus ambulatory heart rates in 839 hypertensive subjects participating in the Hypertension and Ambulatory Recording Venetia Study (HARVEST). A 24-hour heart rate was recorded twice; this procedure was repeated three months later. Reproducibility was better for ambulatory than for office measurement, and was greater for 24-hour than for daytime heart rate, and lowest for night-time heart rate. Reproducibility of office heart rate was impaired above 85 bpm, and was poorer in subjects with more severe office hypertension. A small but significant decrease in average daytime (−1 bpm, \( P < 0.0001 \)) and virtually no change in night-time heart rate (−0.3 bpm, NS) were observed at repeat recording. Heart rate reproducibility indices were related to the extent of the heart rate and blood pressure white-coat effect, but did not vary according to age, gender, body mass index, day-night blood pressure difference, or alcohol or tobacco use. Results indicate that heart rate recorded over the 24 hours has a better reproducibility than office heart rate, and could thus be a better prognostic indicator than traditional measurement of resting heart rate in the hospital setting. Am J Hypertens 2000; 13:92–98 © 2000 American Journal of Hypertension, Ltd.

KEY WORDS: Heart rate, ambulatory monitoring, reproducibility, blood pressure, variability, HARVEST.

There is mounting evidence that heart rate is a good predictor of future development of hypertension¹ and that it is associated with a greater risk of cardiovascular and all-cause mortality.²⁻⁴ These observations are reinforced by recent studies in which many confounding factors were controlled.⁵⁻⁷ However, it should be noted that in almost all of these studies, heart rate was calculated from one or a few measurements taken in the clinic. Heart rate is a highly variable physiologic phenomenon influenced by a variety of environmental stimuli.⁸ Thus, it is possible that the association between heart rate and other clinical variables of interest has been underestimated in most studies. A better estimate of the subject’s usual heart rate could be acquired from 24-hour recordings, but no data are available as to the reproducibility of this heart rate measure, compared with office heart rate.

The Hypertension and Ambulatory Recording Venetia Study (HARVEST) trial is a multicenter study that aims to evaluate the predictive role of 24 hour...

versus office blood pressure for the development of sustained hypertension in subjects with borderline to mild hypertension.9 Two baseline 24-hour recordings of blood pressure and heart rate are performed three months apart. This article builds on the data collected up to this point, and explores the issue of the reproducibility of office heart rate versus 24-hour heart rate measures, and of heart rate versus blood pressure measures in HARVEST participants. We also aimed to assess differences in reproducibility of heart rate in subjects grouped by day-night blood pressure difference or by the extent of their white-coat effect.

METHODS

Subjects  The study was carried out in 839 subjects aged 18–45, with diastolic blood pressure (DBP) between 90–99 mm Hg or isolated systolic hypertension (systolic blood pressure (SBP) > 140 mm Hg and DBP < 90 mm Hg).9 Mean age was 33 ± 9 years in 606 men, and 36 ± 8 years in 233 women. Other subject characteristics and the methods employed in the study have been described extensively elsewhere.10,11 Demographic and clinical data of subjects are reported in Table 1.

Office and 24-hour heart rate and blood pressure
Office heart rate and blood pressure were measured three times after a 5-minute rest in the supine position. The mean of the three readings was defined as the office measurement. Twenty-four-hour measurement was obtained with either the A&D TM-2420 model 7 (A&D Co. Ltd., Tokyo) or the ICR SpaceLabs 90207 (SpaceLabs, Redmond, WA). Both devices were validated12,13 and shown to find comparable results.11 The instrumentation was always applied and removed in the hospital. Patients were asked to avoid strenuous physical activity and to remain motionless while the device was in operation. They were invited to perform the same pattern of activity during both recordings. Patients were asked to go to bed not later than 11 p.m. Heart rate and blood pressure were measured every 10 minutes during waking hours (6 a.m. to 11 p.m.) and every 30 minutes during the night (11 p.m. to 6 a.m.). Other details on procedures and the analysis of the recordings have been reported elsewhere.10,11

Data Analysis  Measurements recorded during the ambulatory period were stored on a personal computer and screened for editing of artifactual values based on previously described criteria.10,11 Only recordings containing error measurements < 20% were considered acceptable for evaluation. A mean of 126 ± 16 unedited readings and 109 ± 20 valid readings were obtained during the 24 hours. The average of the edited heart rates and blood pressures was used as the ambulatory measurement for each period of recording. Average 24-hour, daytime (6 a.m. to 11 p.m.) and night-time heart rates and blood pressures were calculated, as well as day-night differences.

White-coat effect was defined as the difference between office and mean daytime values. Day-night differences and white-coat effect were calculated both as absolute values and values corrected for the level of mean daytime values. Subjects were defined as sustained hypertensives if daytime SBP was higher than 135 mm Hg or daytime DBP was higher than 85 mm Hg; otherwise, they were defined as white-coat hypertensives. Subjects with a night-time heart rate fall or an SBP fall > 10% of daytime values were considered non-dippers; otherwise, patients were defined as dippers.14

Statistical analysis  Baseline and repeat periods of recording were compared with the Student’s t test for paired observations. The Pearson test was used for correlations, and reproducibility was assessed using the Bland-Altman approach.15 Change between duplicate recordings was calculated by subtracting the first from the second recording, taking into account the sign of the difference. Consistency was obtained by calculating the difference between baseline and repeat recordings, disregarding the sign of the difference. Repeatability was defined as twice the standard deviation of the changes between the two repeated recordings. To compare the reproducibility of different variables, the maximal biological variation (MBV) of the variables was calculated (twice the standard deviation of the between-measurement differences, divided by four times the standard deviation of the mean of the two duplicate recordings).16 To assess the between-group differences in heart rate consistency, a multiple linear regression model (ANCOVA) was used that included coffee consumption, physical activity status, smoking, age, weight, height, gender, and systolic blood pressure. Differences were considered statistically significant at p < 0.05.

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alcohol intake, smoking, age and sex as covariates. Data are mean±SD unless specified. Significance was taken as a probability value < 0.05.

RESULTS
An average number of 89±16 valid readings were obtained during daytime, and 20±7 readings at night. Baseline and repeat heart rate values by gender are reported in Table 1. Correlation coefficients between baseline and repeat measurements were smaller for office than for all ambulatory periods (Table 2). In Figure 1, changes of heart rate from the first to the second measurement are plotted versus the mean of the two measurements. Limits of agreement (95% CI) were wider for office heart rate (−21.9 to 18.0 bpm) than for 24-hour heart rate (−13.0 to 11.6 bpm).

Change, consistency, repeatability and MBV for office heart rate and the various periods of the ambulatory measurement are reported in Table 3. All indices of reproducibility were better for the ambulatory measurement than for the office measurement. Within ambulatory data, all changes from baseline to repeat recording were ≤1 bpm. A small significant fall was observed for daytime heart rate, and a negligible one for night-time heart rate. Consistency, repeatability and MBV were better for 24-hour than for daytime heart rate. The poorest values were observed for night-time heart rate.

Changes in office heart rate from the first to the second measurement were significantly correlated with the level of baseline office heart rate (r = 0.55, P < 0.0001) and SBP (r = 0.17, P < 0.0001).

When subjects were divided according to whether they had an office heart rate ≤ 85 bpm or > 85 bpm, subjects with heart rate > 85 bpm had a poorer consistency than subjects with heart rate ≤ 85, while no significant differences emerged between the two groups for ambulatory heart rates (Table 4). The repeatability index was also better for subjects with lower office heart rate (18.1 bpm) than for those with higher heart rate (19.7 bpm). The respective values for 24-hour heart rate were 12.2 bpm and 12.6 bpm.

No significant differences in consistency were found between the genders for either office or ambulatory heart rates. Furthermore, reproducibility indexes did not vary according to age, body mass index, smoking or alcohol use (data not shown).

Change, consistency, repeatability and MBV for office and 24-hour SBP were similar to those for office and 24-hour heart rate (Table 5). For both pressures, MBV data were similar to those for office and 24-hour heart rate. Similar results were obtained for DBP (data not shown). The reproducibility of the white-coat effect and of the day-night difference was poorer than that for the average ambulatory periods for heart rate, SBP, and DBP.

Heart rate variability according to white coat effect and dipping status Changes in office heart rate from the first to the second measurement were significantly correlated with the extent of the heart rate and SBP white-coat effect, either when the sign of the differen-
ence was taken into account \( r = 0.51, P < 0.0001, \) and \( r = 0.16, P = 0.001, \) respectively) or it was disregarded \( r = 0.25, P < 0.0001, \) and \( r = 0.14, P = 0.024, \) respectively). In the subjects divided according to whether they had white-coat or sustained hypertension, office heart rate change and consistency differed between the two groups (Figure 2). Wider variations in office heart rate (from the first to the second measurement) were observed in the white-coat hypertension group. Heart-rate consistency for the ambulatory measurement did not vary with the white-coat or sustained hypertensive conditions (Table 4).

No correlation was found between heart rate change and consistency and the day-night heart rate or blood pressure difference. In the subjects grouped according to whether their day-night heart rate or SBP difference was \( \geq 10\% \) or \( <10\% \), no differences in heart rate change and consistency were observed.

**DISCUSSION**

The importance of heart rate for the development of hypertension and of cardiovascular morbidity has become increasingly recognized.\(^1\)\(^-\)\(^6\) In spite of the evidence provided by numerous studies, until recently physicians tended to overlook this important risk factor, and heart rate has been long ignored, or viewed as a benign prognostic sign. Recently, interest has been aroused by the introduction of new antihypertensive drugs\(^7\)\(^,\)\(^8\) capable of decreasing heart rate without affecting the patient’s metabolic profile, an effect which has been shown to occur with beta-blocking agents. Whether antihypertensive agents that reduce the heart rate may have a more favorable impact on the morbidity and mortality of hypertensive subjects, compared with drugs that do not reduce heart rate, is likely to be the focus of future large intervention studies. However, no data exist to indicate whether, in such studies, heart rate measured over 24 hours should be preferred to resting heart rate measured in the clinic. Like ambulatory blood pressure, 24-hour heart rate might afford greater precision of measurement than can be achieved using casual measurement. In this respect, ambulatory heart rate might be particularly useful for clinical research by reducing the number of subjects required\(^9\) and by demonstrating various treatment effects that office heart rate could not detect, due to the timing of measurement and lack of statistical power.

The results of the present study show that ambulatory heart rate is more reproducible than heart rate

### Table 3. Reproducibility Indexes for Heart Rate Measured in the Office and with 24-Hour Ambulatory Recording

<table>
<thead>
<tr>
<th>Period</th>
<th>Change</th>
<th>P</th>
<th>Consistency</th>
<th>Repeatability</th>
<th>MBV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR office</td>
<td>2.0</td>
<td>&lt;0.0001</td>
<td>7.8</td>
<td>19.9</td>
<td>62</td>
</tr>
<tr>
<td>HR 24-hour</td>
<td>0.7</td>
<td>0.001</td>
<td>4.7</td>
<td>12.3</td>
<td>39</td>
</tr>
<tr>
<td>HR day</td>
<td>1.0</td>
<td>&lt;0.0001</td>
<td>5.1</td>
<td>13.3</td>
<td>40</td>
</tr>
<tr>
<td>HR night</td>
<td>0.3</td>
<td>ns</td>
<td>5.6</td>
<td>15.0</td>
<td>49</td>
</tr>
</tbody>
</table>

Change is first minus second measurement considering the sign of the difference (a positive value means a decrease over time). Consistency is difference between the two measurements disregarding the sign of the differences. Repeatability is twice the standard deviation of the between-measurement differences. MBV indicates maximal biological variation of the variable. HR indicates heart rate in beats per minute.

### Table 4. Consistency of Office and Ambulatory Heart Rate in the Subjects Divided by Office Heart Rate Level, by Gender and by Their White Coat or Sustained Hypertensive Condition

<table>
<thead>
<tr>
<th></th>
<th>Office</th>
<th>24-hour</th>
<th>Daytime</th>
<th>Night-time</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR ( \leq 85 \text{ bpm} ) (n = 717)</td>
<td>7.0 ± 0.2</td>
<td>4.6 ± 0.2</td>
<td>5.1 ± 0.2</td>
<td>5.6 ± 0.2</td>
</tr>
<tr>
<td>HR &gt; 85 \text{ bpm} ) (n = 122)</td>
<td>12.1 ± 0.6</td>
<td>4.9 ± 0.4</td>
<td>5.4 ± 0.4</td>
<td>6.1 ± 0.5</td>
</tr>
<tr>
<td>Males (n = 606)</td>
<td>7.6 ± 0.3</td>
<td>4.6 ± 0.2</td>
<td>5.2 ± 0.2</td>
<td>5.4 ± 0.2</td>
</tr>
<tr>
<td>Females (n = 233)</td>
<td>8.1 ± 0.5</td>
<td>4.7 ± 0.3</td>
<td>4.9 ± 0.3</td>
<td>6.1 ± 0.4</td>
</tr>
<tr>
<td>Sustained hypertensives (n = 229)</td>
<td>6.9 ± 0.4</td>
<td>4.5 ± 0.3</td>
<td>5.0 ± 0.3</td>
<td>5.7 ± 0.3</td>
</tr>
<tr>
<td>White coat hypertensives (n = 610)</td>
<td>8.1 ± 0.3</td>
<td>4.7 ± 0.2</td>
<td>5.2 ± 0.2</td>
<td>5.6 ± 0.2</td>
</tr>
</tbody>
</table>

Data are mean ± SEM. Consistency is the difference between baseline and repeat measurement disregarding the sign of the difference. Subjects with daytime blood pressure lower than 135/85 mmHg were defined as white coat hypertensives, otherwise they were defined as sustained hypertensives. HR indicates heart rate in beats per minute. The covariates used in the models are reported in the Methods.
measured in the clinic. A 39% improvement in the MBV reproducibility index was found for 24-hour heart rate, compared with office heart rate, a difference greater than that observed for 24-hour versus office blood pressure in this and other studies. However, in this study, 24-hour heart rate was calculated from an average of 109 readings, while office heart rate was the average of only three readings. A small decrease in average daytime heart rate (−1 bpm) and virtually no change in average nighttime heart rate were found from the first to the second measurement. The reduction in office heart rate was also modest (−2 bpm), and comparably lower than that found for office SBP. This is in agreement with results from a small sample of subjects studied with intraarterial monitoring, and indicates that a small attenuation of small sample of subjects studied with intraarterial monitoring. This is in agreement with results from a small sample of subjects studied with intraarterial monitoring.

A body of evidence indicates that the predictive power of heart rate for cardiovascular morbidity and mortality is greater in men than in women. This might be due to a greater variability of heart rate in the latter. However, present results show that the reproducibility of both clinic and ambulatory heart rates did not vary according to gender.

Smoking or alcohol use could be important sources of increased heart rate variability over time. Tobacco and alcohol are known to affect heart rate, and changes in habits related to the use of these substances from one day to another could impair heart rate reproducibility. However, our finding of a similar heart rate reproducibility in smokers and non-smokers, and in alcohol drinkers and abstainers, does not support this hypothesis.

Besides average 24-hour blood pressure, the white-coat effect and the day-night blood pressure difference have been shown to predict target organ damage. However, it is still debatable whether these variables are really associated with cardiovascular complications in hypertension. The results of the present analysis clearly show that the reproducibility of the white-coat effect and of the day-night difference is worse than that of the mean 24-hour period for both blood pressure and heart rate. Moreover, greater heart rate changes were observed in white-coat hypertensives than in sustained hypertensives over the three-month period. This casts some doubt on the clinical utility of these measures and suggests that at least two ambulatory monitorings should be made to classify the subjects as white-coat or sustained hypertensives, and dippers or non-dippers, respectively. Subjects with white-coat hypertension have been shown to have greater blood pressure and heart rate liability than subjects with sustained hypertension. Thus, greater between-measurement variation should be expected in the former. The results of the present study show that this was the case, as greater changes were observed in white-coat hypertensives over the three-month period.

Dippers and non-dippers had similar heart rate changes from the first to the second assessment, and
no relationship was found between indices of heart rate variability and day-night blood pressure difference.

A possible limitation of this study was that ambulatory heart rate was calculated from intermittent measurements and not from beat-to-beat recordings. However, Parati et al. showed that intermittent and continuous measurements of heart rate provide comparable results. The intermittent method allows simultaneous assessment of heart rate and blood pressure. Only a few blood pressure monitoring devices are provided with continuous ECG recording, a characteristic that implies a considerable increase in cost.

REFERENCES


