正常血圧者における24時間連続2回の血圧・脈拍パターンの再現性

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Repeatability in Two Consecutive 24-Hour Blood Pressure and Heart Rate Patterns in Normotensive Subjects

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Abstract

The present study analyzes the 24-hour patterns of blood pressure (BP) and heart rate (HR) in an illustrative sample of clinically healthy adults who were monitored over two consecutive days. The aim is to provide group -qualified measures for the discrete and periodic variability of BP and HR, in addition to its use as a control of the short-term repeatability of such monitoring. One hundred and ninety-two clinically healthy subjects volunteered, and consisted of 75 males and 117 females, ranging in age from 18 to 86 years. The estimates refer to 1. time-qualified distribution, and 2. rhythmometric parameters. The biometric estimates indicate the existence of nychtohemeral variability and circadian rhythmicity in the 24-h BP and HR physiologic pattern. Such a time-dependent pattern is repetitive over two consecutive days of monitoring. Such a day to day repeatability in the daily BP and HR seems to be a characteristic feature of the normotensive status. The biometric methodology illustrated herein may thus be used to more advantageously describe the 24-h BP and HR pattern in stratified samples of subjects.

Key words: biostatistics, blood pressure monitoring, chronobiology, circadian rhythms, hypertension, normotension.

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INTRODUCTION

Even though the clinicians are used to measure the blood pressure (BP) by means of the Riva Rocci sphygmomanometer from about 90 years, they must agree that the validity of this approach is questionable because of the fact that such "casual" measurements cannot accurately demonstrate the inherent variability shown by the hemodynamic variables during the 24 -hour span[12-14]. Presently, the non-invasive automated BP monitoring seems to be an alternative technique that the clinicians are obliged to use whether they want to evaluate the within-day variability of BP with the medical purpose of diagnosing some of its deviant conditions.

It must, however, be stressed that the use of the automated monitoring raises consistent problems which are prominently related to the biometric exploration, considering the within-day BP variability also expresses the circadian rhythm[3, 5, 6, 7, 10].

Methodologically, an accurate biostatistical analysis should, thus, contemplate the biometry of the within -day BP variability not only as a sequence of discrete values but also as a phenomenon rhythmically

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oscillating within a 24-hour period.

This study is aimed at providing a biometric methodology to investigate the BP time series in given groups of stratified subjects, by showing the appropriate procedures applied to an illustrative sample of clinically healthy subjects.

MATERIALS AND METHODS

Subjects and Protocol

One hundred and ninety-two clinically healthy subjects volunteered and gave their informed written consent for this study. They included 75 males and 117 females, ranging in age from 18 to 86 years.

The non-invasive ambulatory BP monitoring was performed with the subjects free to follow their normal routine lifestyle. They were only requested not to do any extraordinary activities which could induce an excessive reaction of the cardiovascular apparatus. The monitoring was performed by means of a non-invasive automated recorder (ABPM 630, Colin Electronics Co. Ltd., Komaki City, Japan) programmed to take the sphygmomanometric measurements (oscillometric technique) of the systolic and diastolic BP and heart rate (HR) at 30 minute intervals over two consecutive days.

Data Series Analysis

Both the BP and HR time series were processed by means of the numerical and analytical procedures of biometry. The numerical method was used to compute the time-qualified measures of the central location and dispersion with reference to the temporal qualification of the sampled sphygmomanometric values (Numerical Temporal Biometry). The analytical method (Analytical Temporal Biometry) was used to compute the parameters of the BP and HR circadian rhythm, using the Single Cosinor analysis with both mono-component and three-component models of periodic regression[9]. The three-component harmonic model was used as the variance since the variance by regression is much more concordant with that of the 24-hour BP profile which is asymmetric in its variation around its time-qualified mean. In detail, the Single Cosinor method is actually a periodic regression analysis which fits a 24-hour cosine curve to raw data and defines the best fitting waveform profile by means of the least squares method. The Single Cosinor procedure in its mono-component model uses the formula

$$Yt = M + A\cos\left(\frac{2\pi}{24}\times t + \phi\right)$$

where M (Mesor, acronym of midline estimating statistic of rhythm) is the 24-hour adjusted mean, A (amplitude) is the extent of the oscillation from M, (acrophase) is the timing of the crest with reference to local midnight, t is a fractional time of the period (TAU), 2/TAU is the angular frequency (ω).

The Single Cosinor procedure was a three-component model using the formula

$$Yt = M + A_1\cos\left(\frac{2\pi}{24}\times t + \phi_1\right) + A_2\cos\left(\frac{2\pi}{24}\times t + \phi_2\right) + A_3\cos\left(\frac{2\pi}{24}\times t + \phi_3\right)$$

where A_1, A_2, A_3 and ϕ_1, ϕ_2 and ϕ_3, represent the amplitudes and the acrophases of the harmonic waves over periods of 24-hours, 12-hours and 8-hours, respectively.

The group-related measures for M, A and ϕ were computed using the Population-Mean Cosinor[8]. The method computes the confidence limits as Standard Error (SE) for M, and 95% Confidence Limits (95 % CL) for A and ϕ.

The statistical comparisons between the estimates of the first and second day of monitoring were made by means of Student's t test[1, 17] and Bingham's test[4], the latter was also specific for the rhythmometric parameters.

RESULTS

The results are presented according to the order of their statistical analysis.

Numerical Temporal Biometry

Table I displays the time-qualified measures of central location and dispersion of the non-detemporalized BP and HR values. According to the tabulation, it can be said that the time-qualified values exhibit a nychtohemeral variability with a nocturnal decline. A t test for the equality of the time-qualified

Table I. Time-Qualified Mean and Standard Deviation for the 24-Hour Systolic (S), Mean (M) and Diastolic (D) Blood Pressure (BP), and Heart Rate (HR) Pattern in Clinically Healthy Adults Non-Invasively Monitored over Two Consecutive Days.

Time	Day of Monitoring							
(Clock Hours)	1				2			
	SBP	MBP	DBP	HR	SBP	MBP	DBP	HR
00.30	109±16	81±15	63±11	64±10	108±15	80±13	62±10	63±11
01.00	107±15	78±13	61±10	63±11	106±15	79±14	61±11	63±12
01.30	106±14	77±12	60±10	62±11	105±17	78±17	59±12	62±12
02.00	105±15	77±14	59±11	61±12	105±16	76±13	58±11	60±9
02.30	104±14	76±13	58±10	60±11	103±18	76±16	58±12	62±13
03.00	104±17	76±15	58±11	60±11	103±19	76±17	57±15	61±10
03.30	103±15	75±13	57±10	59±10	103±18	75±15	57±14	60±10
04.00	103±15	75±12	57±10	59±10	103±15	75±15	57±10	60±12
04.30	104±15	76±13	58±10	60±11	103±17	75±14	57±12	60±11
05.00	104±16	76±14	58±10	60±12	102±18	76±14	58±12	60±12
05.30	104±17	77±14	59±11	62±13	103±17	76±14	58±11	60±11
06.00	106±16	78±13	60±11	61±13	104±16	76±15	58±11	62±13
06.30	106±16	76±14	61±11	61±12	107±17	78±15	59±12	63±13
07.00	108±18	80±16	62±12	64±14	106±19	78±17	60±12	63±13
07.30	108±17	80±16	62±12	65±16	107±19	79±16	60±12	63±14
08.00	108±18	81±16	63±12	66±16	107±20	80±19	61±16	65±15
08.30	109±18	82±17	63±13	67±17	107±21	79±16	61±14	66±15
09.00	109±17	81±16	63±13	67±17	109±18	81±16	62±13	65±15
09.30	110±18	83±17	64±13	68±16	108±17	81±16	62±13	68±17
10.00	111±19	84±17	65±13	70±16	110±21	82±18	63±14	68±18
10.30	113±21	85±18	66±13	71±17	109±19	82±18	63±13	68±16
11.00	113±19	85±18	66±13	72±17	110±18	83±17	64±13	70±16
11.30	114±18	86±16	66±12	73±16	111±20	84±19	65±14	73±17
12.00	114±17	87±16	66±12	76±16	113±18	85±17	65±13	73±15
12.30	115±18	88±16	67±12	78±16	115±19	87±18	67±14	75±16
13.00	116±19	89±16	68±12	79±16	115±19	87±17	68±13	76±18
13.30	118±19	89±16	69±12	80±15	115±17	88±16	68±12	78±15
14.00	117±19	90±17	69±12	81±15	115±17	88±15	68±12	81±17
14.30	118±17	91±15	70±11	80±15	117±18	91±16	69±12	80±15
15.00	119±18	91±16	70±11	81±15	117±16	89±16	68±12	81±16
15.30	119±17	91±15	70±12	81±14	118±19	90±16	69±13	80±14
16.00	117±18	91±15	69±12	82±14	117±17	90±15	69±12	82±15
16.30	119±16	92±15	70±10	82±14	118±15	90±14	70±11	82±15
17.00	119±17	92±16	71±11	82±15	119±17	91±15	70±12	84±17
17.30	119±19	92±16	71±12	83±16	118±19	91±17	70±13	82±15
18.00	120±17	92±15	71±12	81±15	119±17	90±14	70±11	81±15
18.30	118±17	91±14	70±11	80±13	118±17	92±17	70±12	81±15
19.00	119±17	92±16	70±12	79±13	118±17	91±14	70±10	80±13
19.30	117±15	90±14	69±10	78±13	117±17	91±15	70±12	80±13
20.00	118±16	90±14	69±12	78±12	117±16	89±15	69±11	79±12
20.30	119±17	90±15	69±11	78±13	116±14	88±13	69±10	80±13
21.00	118±15	91±14	69±11	78±12	115±17	88±15	69±12	78±12
21.30	119±17	91±15	70±12	79±13	117±18	90±15	70±12	80±13
22.00	118±16	90±16	70±12	79±13	117±17	88±15	69±10	79±13
22.30	118±18	92±15	71±12	80±15	118±15	90±14	69±11	81±14
23.00	119±17	91±15	71±12	80±14	117±16	90±14	69±11	82±13
23.30	122±18	93±14	72±12	81±15	117±17	90±15	70±11	83±15
24.00	122±18	94±18	73±12	84±17	118±16	91±16	71±10	83±12

Values rounded to the nearest unit, and given in mmHg for BP, and beats/min for HR.

values, as well as the daily (from 00:00 to 24:00), diurnal (from 07:00 to 23:00) and nocturnal (from 23:00 to 07:00) means failed to demonstrate any significant difference between the time series of the two consecutive monitorings, thus demonstrating the 24-hour BP and HR pattern repeats to almost invariably show the temporal sequence over the short time of 48 hours in normotensives.

Analytical Temporal Biometry

Table II depicts the results by a Cosinor analysis with respect to the first, second and third harmonic component. According to the P values, it can be derived that a highly statistically significant circadian rhythm characterizes the 24-hour BP and HR pattern on both days of monitoring. According to the rhythmometric properties, it can be inferred that the BP and HR circadian rhythm shows comparable properties on days 1 and 2 of the recording. Bingham 's test for the equality of the rhythmometric parameters failed to find any statistical difference, thus demonstrating the 24-hour BP and HR pattern to repeat almost unchanged its periodic structure over the two days of observing normotensives.

DISCUSSION

The present study shows the biometric approach to the within-day variability of BP and HR, to be feasible using appropriate methods in order to assure as much biometric information as possible.

The first approach to the time-qualified raw data is to demonstrate whether or not BP and HR show a repeating pattern over the 24-hour scale in a short term distance. As a matter of fact, the time-qualified mean values of BP and HR were not found to be significantly different over the two days of recording.

However, the comparability of the temporal averages does not imply that BP and HR preserved unchanged the properties of their own circadian rhythm over the two days of observation.

The second approach to the time-qualified series is mandatory to explore the eventual changes in the rhythmic properties, considering that some human studies emphasize the fact that the BP and HR circadian rhythm shows an oscillatory crest invariably located in the postmeridian hours of the day[3, 5, 6, 7, 10].

Interestingly, this same phenomenon was observed for the BP and HR circadian rhythm that was estimated in this study. As far as the reproducibility is concerned, the rhythmometric approach is essential to see that none of the oscillatory parameters was significantly changed between the first and second monitoring periods, thus suggesting that the 24-hour BP and HR pattern shows on the short distance of two days a circadian rhythm that is almost stable.

It is important to note that the present study is

Table II. Cosinor-Derived Rhythmometric Estimates for the 24-Hour Systolic (S), Mean (M) and Diastolic (D) Blood Pressure (BP), and Heart Rate (HR) Pattern in Clinically Healthy Adults Non-Invasively Monitored over Two Consecutive Days.

Day of Monitoring	Variables	P	Mesor (±SE)	First Component		Second Component		Third Component	
				Amplitude (95%CL)	Acrophase (95%CL)	Amplitude (95%CL)	Acrophase (95%CL)	Amplitude (95%CL)	Acrophase (95%CL)
1	SBP	<0.001	115 (±1)	7 (6;8)	-228 (-223;-233)	2 (1.5;2.5)	-278 (-274;-282)	2 (1.5;2.5)	-282 (-278;-286)
	MBP	<0.001	87 (±1)	7 (6;8)	-227 (-223;-232)	2 (1.6;2.4)	-274 (-269;-279)	2 (1.5;2.5)	-286 (-281;-291)
	DBP	<0.001	70 (±1)	6 (5;7)	-228 (-224;-232)	2 (1.5;2.5)	-278 (-274;-282)	2 (1.6;2.4)	-282 (-278;-286)
	HR	<0.001	73 (±1)	10 (9;11)	-213 (-213;-219)	1 (0.6;1.4)	-277 (-272;-282)	1 (0.5;1.5)	-279 (-275;-283)
2	SBP	<0.001	115 (±1)	8 (5;11)	-236 (-228;-249)	2 (1.5;2.5)	-269 (-265;-273)	2 (1.6;2.4)	-284 (-280;-290)
	MBP	<0.001	87 (±1)	7 (5;9)	-234 (-227;-245)	1 (0.5;1.4)	-282 (-277;-287)	1 (0.6;1.4)	-271 (-266;-276)
	DBP	<0.001	66 (±1)	6 (4;8)	-237 (-229;-250)	1 (0.6;1.4)	-269 (-265;-273)	1 (0.5;1.5)	-279 (-275;-283)
	HR	<0.001	74 (±1)	11 (10;13)	-220 (-215;-225)	1 (0.6;1.5)	-219 (-214;-224)	1 (0.5;1.5)	-270 (-265;-275)

Values rounded to the nearest unit; P = statistical significance for rhythm detection level; Mesor and Amplitude given in mmHg for BP, in beats/min for HR; Acrophase given in negative sexagesimal degrees (360 Degrees = 24-h); SE = Standard Error for the Mean; 95%CL = 95% Confidence Limits.

aimed at showing which can be an appropriate methodology for the biometric analysis of the non-invasive ambulatory BP monitoring in clinical medicine. Such a methodology was illustrated on a sample of clinically healthy subjects independently of any stratification by age and gender. Obviously, the biometric approach described herein can be applied to any kind of stratification, but it was beyond the scope of this study to demonstrate all samples of stratifications by age and gender. In our opinion, it was most fundamental to demonstrate that the suggested methodology can help the clinicians to explore the discrete and periodic variability of the within-day BP and HR variability by means of very reliable explanatory parameters. As a matter of fact, all the computed biometric estimates showed a short-term repeatability. It can therefore be reasonably argued that the suggested methodology is really suitable for evaluating the 24-hour BP and HR values that clinicians are now exploring by means of non-invasive ambulatory monitoring. Moreover, prolonging the non-invasive automated BP monitoring for 48 hours can also rule out a substantial influence of the circaseptan (about 7-day periodicity) variability because the BP and HR occur in relation to the social routines of humans during the week[2, 19].

It must be remarked that clinical medicine in an increasing number of circumstances tends to replace the"casual"sphygmomanometry with the non-invasive automated BP monitoring, in virtue of the fact that a serial sampling is certainly more informative for describing and interpreting the physiological and unphysiological within-day variability of BP and HR[11, 15, 16, 20]. The present study, however, shows that the non-invasive automated BP monitoring has to be routinely investigated by means of an unabridged methodology in order to interpret the 24-hour BP and HR pattern not only as a temporal sequence of discrete values but also as a periodic phenomenon, having well defined physiological parameters.

As a final comment, it is important to reemphasize that the comprehensive biostatistical approach found mostly stable estimates in each sector of the biometric evaluation in the normotensive subjects. Therefore, one can assume that the day to day repeatability of the biometric estimates in 48-h non-invasive ambulatory BP monitoring might be one of the characteristic features of the normotensive regimen. This conclusion seems to be further reinforced by the fact that such a short-term inter-day repeatability is not detectable in patients suffering from hypertension[18].

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