時間生物学的血圧モニタリングに基いた高血圧診断基準の新しい考え方

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Blood Pressure Monitoring and Chronobiometry: New Reference Standards and Definitions Concerning Normotension and Hypertension

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Key words: Blood pressure; Chronobiology; Hypertension; Monitoring; Reference Standards.

Summary

Industrial technology has made the automated monitoring of blood pressure (BP) a practicable reality. Medical chronobiology has made the interpretation of the BP monitoring a clinical concreteness. Thanks to chronobiometry, new reference standards and definitions concerning normotension and hypertension are derived. Accordingly, the BP 24-h patterns can be better quantified in their physiologic and unphysiologic course. The new methodology, thus, allows to minimize both false positive and false negative diagnoses of hypertension.

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Need For Time-Qualified Standards of Blood Pressure

Technological progress in medical instrument automation has dramatically magnified the problem of quantifying and interpreting the temporal variability in biophysical and biochemical phenomena. Most of scientific reports dealing with the 24-h variability, including the 24-h changes of blood pressure (BP), have processed time data series by means of the traditional statistics. This means that the BP 24-h patterns have been prominently quantified in their central location, and frequency distribution.

Basically, this kind of biometry may be regarded as methodologically inappropriate, the procedures failing to analyse time data series in historicity and directionality that characterize their longitudinal evolution. Constitutively, it must be realized that any temporally-ordered sequence of data is composed by a systematic

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component that is ordinarily masked by both aleatory (casual) and occasional (contingent) events (stochastic component). The systematic component invariably indicates that any constitutive value relates with the previous one on a non-stochastic basis. A temporal series is, thus, necessarily a historical and directional sequence whose time points cannot be regarded as independent.

The methodologic inappropriateness of traditional biometry casts its shadow on the clinical interpretation of the BP 24-h patterns. All medical doctors are aware of the fixed (non time-varying) reference threshold for normotension that is recommended by World Health Organization (WHO)\(^6\). The WHO's guidelines are clearly derived via a traditional biometry, their definition being based on the frequency distribution of isolated (casual) BP measurements treated as non-historical but spatial entities (interindividual variability). The limitation of the WHO's standards for interpreting the BP 24-h monitoring is patent. In a situation of variability, a fixed reference cut-off can generate false positive and false negative diagnoses as indicated in figure 1.

All investigators agree that BP shows time-qualified changes along the 24-h span. Furthermore, it is generally admitted that a physiologic BP nyctohemeral curve may show in its 80.000-140.000 beat-to-beat values a certain percentage (less than 11 %) of aberrant tensions (biological noise), that are certainly due to the stochastic component.\(^{10}\) All of this leads to the logical conclusion that normotension should be estimated on time-varying reference standards that are able to remove the masking effect of randomness.

**Chronobiologic Methodology for Reference Standards**

Chronobiology, as the discipline that explores and quantifies the biological time structure, provides a body of biostatistical procedures (chronobiometry) for appropriately constructing time-varying reference standards. Basically, it must be realized that the time-qualified standards have to be derived by BP measurements taken around the clock in each subject (intraindividual variability). The individual series will be interindividually processed for the statistical standardization of population reference limits (desms). Operatively, the construction of desms is made by transforming confidence limits (CL) into tolerance limits (TL). The statistical operation is feasible by correcting the standard deviation (SD) by the t value of the “normal” distribution that relates to a P level of probability \((1 - \alpha)\) for a given degree of freedom (DF), the latter being calculated from the number \((n)\) of samples.\(^{11}\)

The formula is

\[
TL = \text{Mean} + / - SD \times t_{P \left(1 - \alpha\right) \, DF \left(n-1\right)}
\]

Conventionally, the most frequently calculated desms relate to the 90 % tolerance limits (90 % TL). The 90 % TL, thus, represent the region of the distribution expected to include 90 % of values with 90 % of probability.

The first approach of chronobiometry is to descriptively quantify the time-qualified points of the raw data series (Fig. 2). Such a non-inferential (macroscopic) chronobiometry of discrete data\(^{13}\) makes it possible to compute reference desms (macroscopic or non-inferential chronobiologic desms) that relate to time, i.e., merodesms and chronodesms (see ahead).

The second approach of chronobiometry is to resolve and quantify the systematic component of temporal series in order to remove the “biological noise” made by the stochastic data. Such a chronobiometry uses

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**Fig. 1** How fixed reference standard can generate false diagnoses.
**TRANSVERSE ANALYSIS OF CENTRAL LOCATION DOMAIN BY DESCRIPTIVE UNIVARIATE STATISTICS OF TIME-QUALIFIED DATA**

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**LONGITUDINAL ANALYSIS BY POPULATION-MEAN COSINOR OF TIME-QUALIFIED DATA**

**Fig. 2** Statistical determination of the central location and its dispersion in each time-point by a transverse analysis of multiple data series according to macroscopic chronobiometry.

**Fig. 3** Statistical determination of the best fitting sinusoidal wave and its dispersion by a longitudinal analysis of data series according to microscopic chronobiometry.
Analytical models that fit the time series in its longitudinal sequence (microscopic or inferential chronobiometry). Factually, inferential chronobiometry applies the cosinor procedure, a method of periodic regression analysis that fits a cosine function \( Y_t = M + A \cos(2\pi \tau + \phi) \) with a fixed period (\( \tau \)) to raw data using the least-squares minimization (Fig. 3). This method appears to be highly adequate to resolve and quantify the circadian rhythm that takes place along the 24-h span. The inferential chronobiometry is aimed to compute the reference desms for the best-fitting sinusoidal profile, i.e., cosinodesms, and for the computed rhythmometric parameters, i.e., parameterdesms (see ahead). The latter desms relate to 90 % TL for mesor (M, midline estimating statistic of rhythm or rhythm-adjusted mean), i.e., mesordesm; amplitude (A, one half of the extent in the sinusoidal oscillation), i.e., amplitudedesm; acrometron (mesor + amplitude), i.e., acrometrondesm; acrophase (\( \phi \), timing of the oscillatory crest related to local midnight), i.e., acrophasedesm (see ahead).

Interestingly, the cosine function can be used to compute the integral that expresses the area underlying the sinusoidal curve (Fig. 4). The estimate, that is termed Aesor (Area estimating statistic of rhythm), represents a dynamic parameter for measuring a bioperiodic phenomenon in the time course of its systematic component. The 90 % TL for this parameter produce the Aesordesm (see ahead).
Chronobiologic Reference Standards for Blood Pressure

Both the macroscopic and microscopic chronobiologic desms can be derived for the BP 24-h patterns in order to define the "baro-desms". The baro-desms presented here refer to adult individuals of both sexes.

1. Macroscopic or non-inferential chronobiologic baro-desms

Two types of time-qualified baro-desms can reliably standardize the BP 24-h patterns in their physiologic course. The first one relates to baro-merodesms that represent the 90 % TL for BP pertaining to each time-point of the day (Fig. 5). The second one relates to baro chronodesms that represent the 90 % TL for BP as a band of distribution expressing all the time points of the day (Fig. 6). Such time-varying reference standards should replace the fixed threshold given by WHO, as they express the variability of normotension along the 24-h scale.

Fig. 7 Cosinordesms for systolic (S) and diastolic (D) blood pressure (BP) in adults.

Fig. 8 Parameterdesms for blood pressure in adults.

Fig. 9 The Aesor for the circadian rhythm of blood pressure is called Baric Impact.
2. Microscopic inferential chronobiologic baro-desms

As BP is a rhythmic variable \textsuperscript{1,2,3,7,9}, the inferential chronobiometry provides to define the systematic component of the BP 24-h patterns as a sinusoidal wave. Several types of desms can be derived by the waveform profile that represents the BP circadian rhythm. Among them, the baro-cosinordesms that represent the band that includes 90% of oscillatory extent with 90% of probability (Fig.7). The rhythmometric parameters, mesor, amplitude, and acrophase, have their baro-parameterdesms (Fig. 8). Lastly, the Aesor for the BP 24-h patterns (Fig. 9) can be called Baric Impact.\textsuperscript{31} The baro-impactodesm, thus, represents the 90% TL for this parameter (Fig. 10).

Chronobiologic Reference Standards for Blood Pressure as a Function of Age

Chronobiological investigation has incontrovertibly demonstrated that the periodically-arranged biological functions change their rhythmometric properties along life span. This process of rhythmometric adaptation can be called “gerontologic spectroclinia (gerospectroclinia)”, using the term “clinous” as the equivalent of “trend”. Gerospectroclinia can be measured by “cliniospectrometry”, a biometric procedure that uses the linear regression analysis to resolve the relationship between the rhythmometric properties and age. By computing the 90% TL for the gerontological regression curve, the age-related chronobiologic desms for rhythmometric properties can be calculated (geroclinospectrodesms).

Cliniospectrometry for the BP 24-h patterns provides new age-related reference standards, i.e., baro-geroclinospectrodesms (Fig.11). The desms refer to mesor (baro-geroclinomesordesms), amplitude (baro-geroclinamplitudedesms), acrometeron (baro-geroclinacmometrodessms), acrophase (baro-geroclinacrophasedesms), and baric impact (baro-geroclinimpactodesms), and represent with their band, the region including 90% of distribution with 90% of probability for each rhythmometric parameter along life time.

Chronobiologic Definition of Normotension

The new reference standards for normotension already presented, clearly demonstrate that the BP regimen is more accurately explored by adopting the 24-h monitoring in combination with the chronobiologic analysis. The chronobiologic BP monitoring poses, however, fundamental considerations on the definition of “normotension”, taking into account that a temporal series is an entity not only quantitative but also behavioral.

In order to focus on the definition of normotension, attention has to be paid to three illustrative examples that refer to individualized systolic (S) BP 24-h patterns (baro-chronotypes). Figure 12 illustrates a circadian baro-chronotype which is characterized by SBP values that fall within the upper 90% TL. Chronobiologically, the sequence is validated to fluctuate with a circadian rhythm, the properties of which are normal. The Baric Impact is normal. Figure 13 displays a circadian baro-chronotype which shows SBP values that fall within the upper 90% TL. Chronobiologically, the sequence is validated to oscillate with a circadian rhythm, the acrophase of which is concretely shifted. The Baric Impact is normal. Lastly, figure 14 displays a circadian baro-chronotype which is characterized by SBP values that fall within the profile of acceptability.
BARO-CLINOSPECTRODESMS

BLOOD PRESSURE

SYSTOLIC

MESOR

DIASTOLIC

AMPLITUDE

ACROPHASE

ACROMETRON

BARIC IMPACT

AGE (YEARS)

Fig. 11  Clinospectrodesms for blood pressure.
Fig. 12  Circadian chronotype for systolic blood pressure (SBP).

Fig. 13  Circadian chronotype for systolic blood pressure (SBP).

Fig. 14  Circadian chronotype for systolic blood pressure (SBP).
The sequence is, however, monotonous, showing no substantial variation around the clock. Chronobiologically, the occurrence of a circadian rhythmicity is not validated. The Baric Impact is normal.

By adopting the "quantitative" criterion that normalcy for biological variables consists in values that fall within the reference desms, one can argue that none of the above-mentioned circadian baro-chronotypes is abnormal. Consequently, one can conclude that the three curves are an expression of normotension. By adopting the "behavioralistic" criterion that normalcy for biological variables consists in values that follow a physiologic pattern within the reference desms, one can argue that the circadian baro-chronotypes 2 and 3 are not normal. Therefore, one should conclude that the two monitoring are not conform to normotension.

Because of these conflicting conclusions, one must reflect that intrinsic to the "quantitative" criterion there is the postulate that assumes normalcy and abnormality as conditions that are mutually exclusive. The examples presented here, are, however, an evidence convincing that this axioma is not acceptable. Really, the condition of "presumable" normotension may include heterogenous situations, as the BP 24-h patterns may be behaviorally structured to show regular, inverted or abolished circadian fluctuations within the reference desms. Accordingly, one must argue that the criterium to be adopted for defining "normotension" is truly crucial.

Conceivably, it is impossible to assume that normalcy may coexist with the disappearance of a circadian rhythmicity. By analogy, it is hazardous to convey that a shifted circadian fluctuation may be regarded as a physiological bioperiodic oscillation. Basically, one must remember that normalcy for biological events is the mirror that expresses their physiology. This implies that the "behavioralistic" criterium cannot be disregarded when dealing with the normalcy of biological phenomena that are characterized by an identifiable dynamism of periodic type.

Once again, it is important to stress that experimental and clinical physiology invariably denotes that human BP changes with a circadian periodicity. The normalcy for BP is, thus, identifiable with the physiological time structure that characterizes its natural course along the 24-h span. In line with this thought, one must assume that the better way to explore normotension, as a state of normalcy for BP, is the chronobiologic reference standardization.

Adhering to such a "behavioralistic" position, how to classify the hemodynamic conditions expressed by the circadian baro-chronotypes 2 and 3? New nomenclatures and definitions may be tentatively proposed. The concept itself of "normotension" must be redefined.

Normotension is "a hemodynamic condition expressed by an identifiable pattern of time-qualified blood pressure values that fall within the time-varying reference desms, and follow the natural nyctohemeral changes, delineating a circadian fluctuation with a physiologic phase" (Fig. 15). The term "Paranormotension" was derived for the second example to intend "a hemodynamic condition expressed by an identifiable
pattern of time-qualified blood pressure values that fall within the time-varying reference desms, and follow unnatural nyctohemeral changes, delineating an circadian fluctuation with an antiphasic crest” (Fig. 15). Lastly, the term “Pseudonormotension” was adopted for the third example to define “a hemodynamic condition expressed by an identifiable pattern of time-qualified blood pressure values that fall within the time-varying reference desms, and follow unnatural nyctohemeral changes, delineating a non-fluctuating profile due to the abolition of circadian rhythm” (Fig. 15).

**Chronobiologic Indices for Blood Pressure Excess**

In discussing on the clinical meaning of the previous argumentations, two main points must be stressed, i.e., 1. the identification of normotension requires proper criteria; 2. intermediate conditions, such as paranormotension and pseudonormotension, can occur as deviant states that are interposed between normotension and hypertension. Because of this, one must realize that the diagnosis of hypertension requires selective rules that are more complex than the simple exclusion of normotension.

Basically, it must be stressed that the essence of abnormalcy for biological events invariably coincides with the presence of reproducible measures that are not consistent with the reference desms. Taking this principle into consideration, one must convey that the “quantitative” criterium is the principal rule for detecting patent deviations in biodynamic events.

In concrete situations, this criterium has to be mitigated. As already pointed out, a time series is constituted by both stochastic and systematic components. This implies that the abnormalcy in time-varying
series must principally relate to a derangement within the non-casual component. For periodic phenomena, the sinusoidal wave that expresses the systematic “formant” should be preferably adopted for identifying deviations from normalcy. With this intension, Halberg and co-workers have proposed the cosinor-derived waveform profile as a tool for the clinical diagnosis of hypertension, and have suggested new “Inferential Indices of Blood Pressure Excess, IIBPE”.[12,13] In a first instance, the IIBPE were related to the WHO reference threshold (Fig. 16). Subsequently, they were related to the upper 90% prediction chronodess (Fig. 17).

Aim of the IIBPE is to detect whether or not the sinusoidal curve that expresses the systematic component of the BP 24-h patterns, exceeds, with its curvilinear profile, the reference threshold, delineating an area of Hyperbaric Impact (HI or HBI). The presence of this supraphysiological area inequivocably suggests the existence of a systematic regimen of hypertension that is not due to casual elevations in BP. It must be stressed that the equation “Hyperbaric Impact = Hypertension” makes justice of some current opinions. As can be argued, the Hyperbaric Impact, as index of the systematic component, can decide whether or not the deviant values that constitute a BP 24-h monitoring are significant for the clinical diagnosis of hypertension. To be significant, such deviant values have to be non-aleatory, demonstrating that their presence affects the BP time structure in its systematic “core”.

According to the criterium of systematicity, two main considerations can be drawn, i.e., 1. isolated

Fig. 17 Inferential Excess Indices for blood pressure estimated versus the time-varying reference desms (upper 90% prediction chronodess). Methodology called “(Hybrid)-Sphygmochron”. (Courtesy by F. Halberg).

Fig. 18 Inferential Excess Indices for blood pressure estimated versus time-oscillating reference desms (upper 90% prediction cosinor-desms and upper 90% prediction Impactodesms). Methodology called “Analytical Sphygmochron”. 
elevations in BP do not necessarily imply the diagnosis of hypertension; 2. arterial hypertension may be formally regarded as a phenomenon that transcends the simple occurrence of high BP values. As the disorder may attain to the systematic component arterial hypertension may be regarded as disease of the mechanisms that drives the circadian organization of the BP 24-h patterns. In other words, hypertension may be regarded as an expression of chronopathology.

Halberg and coworkers have strongly recommended the use of chronobiologic BP monitoring in clinical practice by proposing the Sphygmochron, a chart used as a personal database for storing the values of the IIBPE.\(^{13,14}\) It must be noted that Halberg's system can be defined a “hybrid model” as it compares the sinusoidal profile with the non-inferentially constructed upper reference limits. For the reasons that will be now explained, a non-hybrid model seems to be preferable. The “Analytical Sphygmochron” suggested by us\(^{15}\) uses the sinusoidal profile, as derived by the Cosinor analysis, and the upper 90% prediction of the cosinor (Fig. 18). Such a totally-inferential (non-hybrid) model provides the advantage not only of computing but also of comparing the Baric Impact that is quantified on the BP 24-h patterns under scrutiny (Individual Baric Impact, IBI), with the upper reference Baric Impactodesm (RBI). Two new inferential indices of BP excess can be, thus, estimated, i.e., 1. Baric Excess (BE), an index that refers to the algebraic difference between IBI and RBI (BE = IBI − RBI); 2. Baric Index (Bln), an index that relates to the ratio between IBI and RBI (Bln = IBI/RBI).

Interestingly, in hemodynamic conditions of normotension, paranormotension and pseudonormotension, BE is 0 or a negative value, while Bln is 1 or a value below 1. This implies that the combination of a positive BE with a Bln higher than 1 may be regarded as an unquestionable sign of hypertension.

**Chronobiologic Definition of Hypertension**

Clinical experience with automated monitoring has definitely confirmed that a certain number of supraphysiological values usually contaminate the BP 24-h patterns of normotensive subjects.\(^{15}\) As the origin of these casual aberrations may be not only occasional but also artifactual, the problem of their depuration may not be solved on an empirical basis. To avoid any arbitrariness, the filter has to be done by means of analytical procedures. For this reason, one may consider the cosinor procedure as the biostatistical tool for non-empirically removing the randomness in the BP 24-h patterns. Factually, the cosinor-derived sinusoidal wave still be properly used to diagnose a newly monitored subject as normotensive or hypertensive.

It must be remarked that the diagnostic role of cosinor-derived sinusoidal wave has suggested Halberg et al.\(^{13,14}\) to coin a nomenclature more adequate for identifying arterial hypertension. Amplitude-hypertension and Mesor-hypertension represent two conditions associated respectively with a sinusoidal curve partially or totally above the upper reference limits for BP (Fig. 19).

The “rationale” for the chronobiologic diagnosis of hypertension is presented here by means of some illustrative examples, taking into consideration that the fitted circadian curve can be called “baro-cosinortype, due to its identifiable role. Figure 20 illustrates a circadian baro-chronotype showing some SBP values that fall beyond the upper 90% reference chronodesm. The circadian baro-cosinortype defines no area of Hyperbaric Impact. The Baric Impact is normal. The computed Baric Excess and Baric Index are respectively negative and below 1. Figure 21 depicts a second circadian baro-chronotype showing SBP values that fall beyond the 90% prediction chronodesm. The circadian baro-cosinortype defines an area of Hyperbaric Impact. Importantly, the Baric Impact is not increased so that the computed Baric Excess and
Fig. 20  Circadian chronotype and cosinortype for systolic blood pressure (SBP).

Fig. 21  Circadian chronotype and cosinortype for systolic blood pressure (SBP).

Fig. 22  Circadian chronotype and cosinortype for systolic blood pressure (SBP).
Baric Index are normal as well. Figure 22 displays a third circadian baro-chronotype showing SBP values that fall beyond the upper 90% TL. The circadian barocosinortype defines an area of Hyperbaric Impact. The Baric Impact is increased. The calculated Baric Excess and Baric Index are respectively positive and higher than 1.

In commenting these patterns, it must be stressed that the first example is a typical monitoring that can be misinterpreted if the BP values are evaluated with limitation to the baro-chronotype. Due to the presence of few BP values that fall beyond the reference desm, one could be induced to pose the diagnosis of Labile Hypertension. Taking the chronobiologic criteria into consideration, one can realize that the abnormally increased BP values are per se unable to generate a Hyperbaric Impact or a Baric Excess. The BP 24-h patterns, thus, simulate a condition of hypertension that actually does not exist. To define such an ambiguous situation, the term “Pseudohypertension” can be used. As far as the second example is concerned, it must be stressed that both mesor and amplitude are quantitatively comparable to those of the previous example. An area of Hyperbaric Impact, however, occurs. The cause for this phenomenon is essentially attributable to a “phase-shift”. In details, the anticipation of the circadian oscillation (phase effect) causes some BP values to exceed their time-quantified reference points. To classify such a hemodynamic condition the nomenclature “Phase-hypertension” was coined. The third example emphasizes the concept that any
abnormal elevation in BP is identified by an area of Hyperbaric Impact. The hypertensive deviation is, however, associated with the positivization of the Baric Excess and the inversion of the Baric Index. This means that high BP may coexist with or without a positive Baric Excess even in the presence of a Hyperbaric Impact. This implies that Analytical Sphygmochron may improve the chronobiologic diagnosis of hypertension, providing the identification of new types. Figure 23 presents this classification and illustrates the alteration pertaining to all IIIBPE.

Taking this biometry into consideration, the following definitions can be done. Pseudohypertension is "a hemodynamic condition expressed by an identifiable pattern of time-qualified blood pressure values that sporadically fall above the upper time-varying reference limit without generating an area of Hyperbaric Impact". Phase-hypertension is "a hemodynamic condition expressed by an identifiable pattern of time-qualified blood pressure values that fall above the upper time-varying reference limit, delineating a partial area of Hyperbaric Impact which is not associated with a positive Baric Excess and an inverted Baric Index". Amplitude-hypertension is "a hemodynamic condition expressed by an identifiable pattern of time-qualified blood pressure values that fall above the upper time-varying reference limit, delineating a partial area of Hyperbaric Impact which is associated with a positive Baric Excess and an inverted Baric Index". Mesor-hypertension is "a hemodynamic condition expressed by an identifiable pattern of time-qualified blood pressure values that fall above the upper time-varying reference limits, delineating a global area of Hyperbaric Impact which is associated with a positive Baric Excess and an inverted Baric Index.

**Chronobiologic Grading of Hypertension**

Until now, the IIIBPE have been regarded as parameters exclusively useful for diagnosing hypertension. In our opinion, they may be usefully exploited for grading hypertension as well. All clinicians know the WHO or WHO/IHS classification that uses diastolic (D) BP to subdivide hypertension into borderline (DBP > 90 = < 95mmHg) or mild (DBP > 90 = <105mmHg), moderate (DBP > 105 = <115 mmHg) and severe (DBP > 115mmHg) subtypes. Leaving intact this staging, and emphasizing the chronobiologic criteria, the following redefinitions can be given. Figure 24 may be a guidance for a better understanding.

Borderline hypertension is "a phase-hypertension expressed by a Hyperbaric Impact which is associated with a negative Basic Excess and a subunitary Basic Index". Mild hypertension is "an amplitude-hypertension that is expressed by a Hyperbaric Impact which is associated with a positive Baric Excess and a mildly increased Baric Index". Moderate Hypertension is "an amplitude-hypertension that is expressed by a Hyperbaric Impact which is associated with a positive Baric Excess and a moderately increased Baric Index". Severe hypertension is "a mesor-hypertension that is expressed by a Hyperbaric Impact which is associated with a positive Baric Excess and a severely increased Baric Index".

**Conclusions**

This presentation deals with new reference standards and definitions concerning normotension and hypertension. The text emphasizes the new knowledges derived by the exploration of the BP 24-h monitoring by means of chronobiologic principles and procedures.

Any observer must convey that the time-qualified standardization has made the interpretation of the BP 24-h patterns a non-empirical process. BP is estimated versus time-varying reference standards. Its normalcy or abnormalcy is, thus, realistically explored, as BP is a time-dependent variable. Further innovations are, however, proposed considering that the BP 24-h changes have a precise time structure which is intrinsically characterized by a waveform oscillation. As the systematic component is masked by aleatory (casual) or occasional (contingent) changes that confer "biological noise", the operative proposition is to chronobiologically analyse the constitutive time structure in order to verify whether the BP 24-h changes
represent a condition of normotension or hypertension.

At the 1988, a concept is clear. The fixed WHO reference guidelines appear to be not appropriate for exploring the BP 24-h patterns in their nyctohemeral variability.

The chronobiologic technique has enormously amplified the exploratory possibilities. The BP 24-h patterns can be now compared with new reference standards of inferential type. The diagnosis of normotension and hypertension can be, thus, posed using criteria that dramatically reduce false positive and false negative assignation. Modern medicine is, thus, urged to update the rules concerning the clinical interpretation of BP values. The complexity of the chronobiologic statistics is not an obstacle to the diffusion of the chronobiologic BP monitoring. All biostatistical procedures have been computerized in a package called Sphygmochronomat.

It is, thus, auspicious that chronobiologic reference standards and criteria will be adopted by WHO, the most competent agency to dictate and uniform consensus in the world of Health Science.

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References


Appendix

Glossary

- ACROMETRONDESM: Band including 90% of acrometron distribution with 90% of probability for a given bioperiodic variable of function (defined in the prefix, e.g., BARO-).
- ACROPHASEDESM: Band including 90% of acrophase distribution with 90%
- AESOR: integral of the area underlying a sinusoidal curve that relate to a bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- AESORDESM: Band including 90% of values related to AESOR with 90% of probability for a given bioperiodic variable or function.
- AMPLITUDEDESM: Band including 90% of amplitude distribution with 90% of probability for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- BARIC EXCESS (BE): Difference between an Individualized BARIC IMPACT (IBI) and the upper 90% prediction Baro-Impactodesm (PBI): BE=IBI−PBI.
- BARIC IMPACT (BI): Integral of the area underlying the sinusoidal profile of the blood pressure circadian rhythm.
- BARIC INDEX (BIN): Ratio between IBI and PBI: BIN=IBI/PBI.
- BARO-Impactodesm: Band including 90% of values for BARIC IMPACT with 90% of probability.
- CHRONOTYPE: Individualized temporal pattern for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- COSINORTYPE: Individualized best fitting cosine curve for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- DESMS: reference standards for population measured via 90% tolerance limits.
- GERO-CLINOACROMETRONDESM: Band of the gerontological regression curve which includes 90% of acrometron values with 90% of probability for a given bioperiodic variable of function (defined in the prefix, e.g., BARO-).
- GERO-CLINOACROPHASEDESM: Band of the gerontological regression curve which includes 90% of acrophase values with 90% of probability for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- GERO-CLINOAESORDESM: Band of the gerontological regression curve which includes 90% of baric impact values with 90% of probability for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
g., BARO-).
- GERO-CLINOAMPLITUDEDESM: Band of the gerontological regression curve which includes 90% of amplitude values with 90% of probability for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- GERO-CLINOMESORTHDESM: Band of the gerontological regression curve which includes 90% of mesor values with 90% of probability for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- GERO-CLINOSPECTRODESMS: Reference standards for population related to age-associated changes in rhythmometric properties for a given bioperiodic variable.
- GERONTOLOGIC SPECTROCLINIA (GERO-SPECTROCLINIA): Age-related trend in rhythmometric properties for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- HYPERBARIC IMPACT (HI): Integral of the area underlying the sinusoidal profile of the blood pressure circadian rhythm, that lies above time-qualified reference values.
- MESORDESM: Band including 90% of mesor distribution with 90% of probability for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- PARAMETERDESMS (PARADESMS): Reference standards for population related to cosinor-derived rhythmometric parameters for a given bioperiodic variable or function (defined in the prefix, e.g., BARO-).
- TOLERANCE LIMITS (90%): Band of the distribution expected to include 90% of values with 90% of probability.

時間生物學的血圧モニタリングに
基いた高血圧診断基準の新しい考え方

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和文抄録

科学技術の発展に伴い、血圧の自動測定が可能になった。また時間生物学的方法を医学の分野に応用することによる血圧測定の解釈は臨床的に確かなものとなってきた。時間生物学的測定により正常血圧と高血圧に関する新たな診断基準や定義が導かれ、それによって血圧の24時間の変動パターンは生理学的あるいは非生理学的な経過に、より良好に定量される。かくして新しい方法論は高血圧症の過剰診断・過小診断の両者を少なくすることを可能にする。