On the use of actigraphy in clinical evaluation of diurnal blood pressure profile

Ambulatory blood pressure monitoring

The assessment of diurnal rhythm (profile) of blood pressure (BP) by ambulatory blood pressure monitoring (ABPM) is now an integral part of clinical practice. There are several objective reasons for this. Humans have normal circadian variability of BP rhythm, with a maximum in daytime hours and a minimum in nighttime hours [29, 39]. From the clinical perspective, diurnal BP profile (DBPP) has a prognostic value for risk stratification, because high systolic pressure and insufficient BP decrease at night are the most important risk factors of cardiovascular complications [30, 41]. Scientific data emphasize that nighttime BP is a stronger predictor of cardiovascular risk than daytime BP, and that more attention should be paid to BP evaluation during sleep in some groups of patients [19]. It is particularly true for persons with sleep disturbances. According to European Society of Cardiology/European Society of Hypertension (ESC/ESH) recommendations on the treatment of arterial hypertension published in 2018, suspected lack of nighttime BP decrease in patients with obstructive sleep apnea (OSA) is a specific indication for ABPM [51]. Therefore, the assessment of diurnal BP rhythm, BP values in nighttime hours, nighttime BP decrease, and detection of nighttime hypertension are indications for ABPM [36, 51]. From the practical perspective, most modern ABPM devices with automatic detection of nighttime decrease values, rate of morning increase, and diurnal BP variability should support the calculation of diurnal BP profile.

ABPM is the main method of measurement of diurnal BP profile. It may seem that it gives the physician comprehensive data on individual DBPP features. However, much attention is now paid to simultaneous registration of ABPM and diurnal motor activity (actigraphy) to receive additional information necessary for the correct interpretation of ABPM results and clinically significant decision-making [8, 9, 18]. Actigraphy is not a new technique; first devices were used in studies on human psychology and physiology in 1950s [42]. However, it remains rather unknown for many cardiologists and, therefore, it is insufficiently popular. This necessitates a discussion on some aspects of its application, particularly for the assessment of diurnal BP profile.

Actigraphy

Actigraphy is registration of motor activity by a device implementing a 3D accelerometer and position sensor (actimeter). Usually, long-time actigraphy is performed, with the patient constantly wearing the device from one day to two weeks. The actimeter is fastened to a moving part of body (wrist, ankle, breast) to enable activation of the recording of the amplitude and time of motion (Fig. 1a). Two-dimensional sensors register both motion and body position, i.e., lying, standing, on the right, or on the left side (Fig. 1b). It should be emphasized that although there are smartphone applications for actigraphy, only validated devices should be used for medical purposes. Computer algorithms process the record and detect periods of relative sleep (no activity) and vigilance (activity). Actigraphs with special analysis of movement pattern software additionally estimate various parameters of objective sleep–wake structure.

ABPM plus actigraphy

Synchronous monitoring of BP, activity, and body position provides the possibility of performing ABPM and actigraphy in the same time segments. It provides information on the state of the cardiovascular system in sleep and vigilance, and on the influence of body position changes and motion on BP and heart rate. The actigraphy in expert ABPM can therefore be used for precise, clock-independent calculation of nighttime and daytime BP, detection of BP changes during sleep, and finding connections between these changes and motor activity, body position, and breath disturbances during sleep, and the state of the autonomic nervous system.

Time-independent methods that reflect current vigilance and sleep are the most reliable for detection of daytime and nighttime periods and blood pressure. It is assumed that a person is vigilant during the astronomic day and is at rest.
and sleeps during the astronomic night. On the basis of the solar diurnal cycle, time-dependent methods of periodization were developed with fixed average daytime and nighttime periods. They differ somewhat with respect to the considered time periods, because concurrence with vigilance and sleep is important [35]. A broad interval with daytime lasting from 7 AM to 10–11 PM and nighttime from 10–11 PM to 7 AM, or a narrower interval with a daytime period from 10 AM to 8 PM and nighttime period from midnight or 1 AM to 6 AM is taken. Daytime and nighttime BP and DBPP values are calculated for these periods.

This general approach does not always reflect the reality of modern lifestyle. Obviously, *sleep* and *night* are not synonyms, and they are not always concurrent. It is well known that the onset of sleep and its duration vary from night to night and from person to person, due to individual behavior, household conditions, and stresses during the day. The duration and onset of sleep are also influenced by other factors, for example seasonal changes of light day [46]. Additionally, it is known that a high proportion of the total population has sleep disturbances (insomnia, hypersomnia, sleep apnea, restless legs syndrome, etc.), with impaired falling asleep, frequent nocturnal arousals, decreased total sleep duration, and impaired sleep quality [10, 22, 52]. It should be noted that the impairment of sleep duration and quality is associated with a higher risk of cardiovascular mortality, especially with arterial hypertension [21, 26, 37, 50]. Another important aspect is social deprivation of nighttime sleep, which is common in the working population especially in shift workers [22]. Fig. 2 shows periods of daytime sleep and nighttime activity in a patient working nightshifts.

To avoid errors in the detection of sleep periods, diaries are used in which patients note the times of falling asleep and arousals [18, 36]. However, these notes are not objective in most populations studied [27, 32]. It was found that the true time of sleep onset and wake differ from the time in diaries by 30 min on average and sometimes by more than 90 min. Fig. 3 shows a significant discrepancy between the rest period (8:15 PM to 7:45 AM, probably sleep) registered by actigraphy and the night period of ABPM based on patient’s diary (11 PM to 7 AM).

Such cases to some extent explain insufficient reproducibility of DBP values [4, 13]. Eissa et al. [11] note that diaries used for the registration of motor activity are adequate only in 71% of patients, which leads to mistakes in classification of patients as non-dippers (less than 10% drop in mean BP during sleep) in 32% of cases. For example, 23% of patients who were considered dippers based on their diaries were actually non-dippers. Butkevich et al. [5] showed that due to the variability of criteria of daytime and nighttime periods, re-classification of the status of patients is inevitable. The difference may be 35–69%.

Muller et al. compared daytime and nighttime BP obtained by simultaneous diurnal actigraphy and by fixed daytime (7 AM to 10 PM) and nighttime (10 PM to 7 AM) periods [34]. It was found that the values of nighttime BP and diurnal index were significantly lower in cases of detection of night by actigraphy. Therefore, a question arises about the correlation of nocturnal BP decrease and BP decrease during sleep, which is important for the assessment of cardiovascular risk. Her-
mida et al. [15–17] demonstrated that BP decrease during sleep confirmed by actigraphy is the most precise prognostic risk marker of cardiovascular events and renal failure in patients with arterial hypertension. The MAPEC prospective randomized blind study, in which 3344 patients were observed for over 5 years to find advantages of chronotherapy of arterial hypertension compared to standard therapy in conditions of outpatient BP control, showed that BP decrease during sleep, and not in fixed periods of astrophysical night, was associated with a risk of cardiovascular events [15]. These results should not be ignored.

A meta-analysis by Taylor et al. [47] on heterogeneity of studies on the prognostic value of diurnal variability of BP pays much attention to the differences in methodological approaches to the measurement of time of sleep and vigilance. It was noted that the most precise results are based on the registration of motor activity. International recommendations on outpatient diurnal BP monitoring [20] published in 2013 state that diurnal BP profile and diurnal index should be based on BP values measured during sleep and not in the astronomical night, and current actigraphy data should be used. It is expressly stated that the conclusions about diurnal BP profile made on time-dependent ABPM should be avoided. However, this is not reflected in the position taken by the ESH [35, 36].

The moderate position of the ESH is probably connected to current technical and methodological limitations and especially to insufficient software for the calculation of BP decrease during sleep. Although actigraphy is an option in modern ABPM measurement devices, DBPP values are automatically calculated from standard nighttime intervals and not sleep periods. This issue can be solved by manual input of sleep time intervals, as in the case of patients’ diaries.

**Sleep disturbances and BP profiles**

The problem of sleep disturbances is well described in reviews [3, 14, 38]. There is a high (35–80%) prevalence of arterial hypertension in OSA and OSA is diagnosed in 40% of patients with hypertension. Both conditions are mutually exacerbating. Similar observations were made in subjects with short sleep duration. According to prospective studies and epidemiological data, the probability of arterial hypertension is 32% higher in persons with short (≤5 h) nighttime sleep [7, 24]. The Monitoring Project on Risk Factors and Chronic Diseases in the Netherlands (MORGEN) and the Prospective Urban Rural Epidemiology (PURE) study that collects data among residents of 25 countries demonstrated that persons with ≤6 h of nighttime sleep have a higher total cardiovascular risk and higher risk of coronary heart disease compared to those who sleep 7–8 h [21, 50]. In case of simultaneous deterioration of sleep quality, these risk indicators increase to 63 and 79%, respectively. Disturbed diurnal BP profile in this category of patients is probably an additional contribution to the increased risk [23, 28].

Actigraphy with the use of special analytical programs enables detection of the time of sleep onset and arousal, duration, effectiveness, and latency of sleep, and arousals and vigilant periods after the onset of sleep. The records may last over a week (sometimes up to two weeks), which increases the informative value of the study and makes the method an exceptional diagnostic tool for patients with...
Fig. 2 - Registration of motor activity (ACT, gray bars, upper panel) and number of body position changes per minute (N., red line, upper panel) as well as ambulatory blood pressure monitoring (ABPM, lower panel) of systolic values (red line), mean values (blue line), and diastolic values (green line) in a nightshift worker. It is shown that sleep corresponds to periods from 12:15 to 17:45 h. The patient is vigilant during a standard night period for ABPM records (23:00 to 07:00 h).

Fig. 3 - A fragment of the record of diurnal motor activity monitoring (ACT, gray bars, upper panel) and number of body position changes per minute (N., red line, upper panel) as well as ambulatory blood pressure monitoring (ABPM, lower panel) of systolic values (red line), mean values (blue line), and diastolic values (green line) in patient R, 53 years old. A discrepancy is shown between the night period detected by ABPM (23:00 to 07:00 h) and sleep period (20:15 to 07:45 h) detected by actigraphy.
sleep disturbances. The gold standard for diagnostics of sleep disturbances is now polysomnographic study, which is expensive and difficult to accomplish in long-term (multiple day) monitoring. Consensus papers state that actimetry can be used as an alternative for OSA diagnostics, as a pre-screening, or if polysomnography is impossible. It is also used to detect circadian sleep disturbances and dyssomnias in people with insomnia, including when this connected with depression, and to detect severe sleep disturbances that require treatment [1, 2, 6, 33, 44].

The use of actigraphy for this purpose is advisable because of significant motor activity during sleep and decreased duration of motionless periods in insomnias [45]. Motor activity in persons with OSA is associated with sleep fragmentation with episodes of obstructive apnea or hypopnea [31]. Sleep fragmentation with motor activity in OSA on the other hand correlates with a decreased respiratory function detected by peak rate [31, 40].

The sensitivity of actigraphy for the detection of arousals in patients with OSA is not high (48% compared with 98% sensitivity for the detection of sleep periods in general) [25]. However, this method is highly (>90%) specific. This means that although actigraphy per se does not detect respiratory disturbances, it can indirectly objectify severe OSA and helps to assess sleep efficiency. The application of actimetry with ABPM may improve the selection of patients for polysomnographic study or cardiorespiratory monitoring, and objectify the analysis of nighttime BP increases [45].

It seems that the detection of restless legs syndrome is of a similar importance for expert evaluation of BP profile. Some studies revealed that both primary and secondary syndrome is associated with arterial hypertension, which is found in 30% of such patients [49]. It was shown that restless legs syndrome is more frequently detected in patients with insufficient nighttime BP decrease, and that they have a more severe form of the syndrome [12, 43, 48].

**Other factors influencing BP profiles**

Actigraphy also helps in revealing other factors that influence blood pressure, for example body position. Clinically significant orthostatic and clinostatic hypotension and hypertension are characterized by a decreased or increased BP after the transition to a standing or a laying position, respectively. A connection also was found between postural or orthostatic BP changes during the day and various profiles of nighttime BP decrease in asymptomatic patients without drug treatment. Postural hypotony and a non-dipping profile deteriorate parameters of cardiovascular risk [13].

For obvious reasons, postural conditions are very hard to detect. Patients rarely measure BP due to sudden sickness on the background of hypotension, which is accompanied by dizziness, weakness, and sometimes syncope. BP measurement by another person is not always possible in such moments, because the episodes are short and transient. Therefore, special examination is required to find the link between BP and postural changes. Actigraphy is absolutely indicated in this case, because comparison of the time of the hypotension episode and registered standing up enables true episodes to be revealed.

Fig. 4 shows an example of the short period of orthostatic hypotension.
Practical aspects
In patients receiving ABPM, actigraphy may help to:
1. monitor the activity and its clinical evolution in an outpatient setting;
2. monitor sleep problems, mainly sleep latency and efficiency.

Research agenda
Studies of patients with ABPM are necessary to:
1. find out whether actigraphy is an efficient tool for monitoring of activity and sleep in an ambulatory setting;
2. investigate actigraphic motor activity during 24 h;
3. explore whether and how altered actigraphic parameters should be treated.

Conclusion
Expert assessment of diurnal BP profile requires a precise and objective daytime periodization to evaluate the individual profile of BP decrease phases and to find the causes of insufficient BP decrease during sleep. To do this, traditional ABPM should be enhanced with methods of motion activity registration, i.e., actigraphy. Analysis of both of the measurements makes it possible to verify sleep and vigilance periods and detect some sleep disturbances, periods of motor activity, and changes in body position connected with BP changes, which are significant parameters of diurnal profile in patients with arterial hypertension.

Compliance with ethical guidelines
Conflict of interest. I. Fietz has received research grants from Actelion, Eisai, Heinen & Lowenstein, Jazz Pharmaceuticals, Philips/Respisom, Resmed, Somnondoet UCBC, Vanda. M. Glos has received a research grant from Phaya. T. Penzel has received research grants from Heinen & Lowenstein, Itamaz, Philips/Respisom, Resmed, Somnondoet was partially supported by Russian Federation Government grant N°075-15-2019-1885. S. Gorokhova, M. Buni-aynan and O. Atkov declare that they have no competing interests. The authors alone are responsible for the content and writing of the paper. All authors have read and approved the manuscript.

For this article, no studies with human participants or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

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