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How to reliably diagnose arterial hypertension: lessons from 24h blood pressure monitoring.

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Abstract

Background: Hypertension is a common condition in modern society. As blood pressure fluctuates with time, a single blood pressure measurement is useless to diagnose hypertension. Nevertheless, no well-defined number of measurements is often used for this purpose. Diagnosis and therapeutic control of hypertension are therefore suboptimal.

Objective: To determine the number and timing of measurements needed to give a trustworthy approximation of an individual's average blood pressure.

Methods: In this observational study 306 clinically indicated 24h ABPM datasets were analysed. Hypertension was defined as a daytime blood pressure mean exceeding 135/85 mm Hg. Kappa coefficients determined the best time of day for measuring blood pressure. The optimal number of measurements was estimated using canonical correlation.

Results: 162 (53%) patients were diagnosed with hypertension. Kappa statistics indicated that measuring during the afternoon gave the best agreement with the 24h blood pressure mean (κ = 0,78). According to canonical correlation, about eight to ten blood pressure readings give enough information for hypertension diagnosis.

Conclusions: Eight to ten blood pressure measurements between 1 and 5 p.m. are sufficient to give a clinically useful approximation of the daytime mean blood pressure and therefore for diagnosing hypertension accurately. Future research should determine the ideal dispersion of measurements and include patient characteristics which could influence the required number and timing of measurements. These results may increase the future importance of telemonitoring in diagnosing hypertension.

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HBPM
24h ABPM
Optimal diagnosis

Introduction

Arterial hypertension is a common disease in present-day society. The Global Burden of Disease Study shows that high blood pressure, with 9.4 million deaths each year, is the biggest single contributor to worldwide deaths. [1] The significant prevalence of hypertension underscores the necessity to correctly diagnose arterial hypertension in order to treat the disease accurately. [1] Blood pressure is not a constant value however but rather fluctuates with time and activities. Furthermore, a greater systolic blood pressure variability correlates with a higher risk of cardiovascular mortality. [1, 2] The diagnosis of hypertension is not reliable when based on a single blood pressure measurement taken in a general practitioner's office. [3, 4] Besides, in a clinical setting blood pressure can be spuriously elevated, a phenomenon known as white coat effect. In contrast to white coat hypertension, one can also suffer from hypertension but have perfectly normal blood pressure values when measured in the practitioner's office. This effect was named masked hypertension. [5, 6] Based on the above, 24h ambulatory blood pressure monitoring (ABPM) has gradually gained more interest in diagnosing hypertension. [1] This method of gathering blood pressure measurements provides a larger number of readings and white coat and masked hypertension phenomena can be diagnosed. Furthermore, one can make an estimate about the 24h blood pressure variability. Ultimately, with 24h ABPM, the efficacy of antihypertensive medication therapy can be assessed. [5, 7]. However, due to practical reasons, 24h ABPM is not often used in clinical practice A great disadvantage is the impact of wearing the monitoring device on a patient's life. Carrying a 24h blood pressure monitor 24 hours is not comfortable, particularly at night. In addition, a 24h ABPM procedure is more expensive than measuring blood pressure in a physician's office. [8].

As an alternative, home blood pressure measurements show a better correlation with blood pressure values obtained from 24h ABPM than office blood pressures do. [7] The European

Society of Hypertension suggests two morning and two eventing blood pressure measurements should be taken at home for three till seven days in a row. There is not much evidence concerning this recording scheme however. [9] Therefore, the aim of this study is to determine the number and timing of measurements needed in the home-setting to reliably approach the 24h blood pressure mean and diagnose hypertension accurately.

Methods

Study design and study population

Patient data for this observational study were obtained from the local heart centre. Initially 408 patients with clinically indicated 24h blood pressure measurements were included. In order to guarantee the quality of the 24h blood pressure measurement, patients with at least 70 per cent of valid measurements were selected. Validity implied 34 blood pressure measurements had been recorded accurately by the device. [4, 5] 306 patients (75% of the study sample) fulfilled the inclusion criteria. All of the ABPM measurements had been taken between 21/05/15 and 04/03/16. Figure 1 illustrates the patient selection for the study sample. Blood pressure values measured during the night were not considered. This was accordant to the purpose of the study to provide a fixed number of blood pressure measurements one should take in the home-setting during the day. Retiring (09:01 p.m. to 00:59 a.m.) and rising (06:01 a.m. to 08:59 a.m.) periods were also eliminated, excluding variations in time spent in bed. Therefore, only blood pressure values measured during the fixed daytime interval 09:00 a.m. - 09:00 p.m. were analysed. [10] The ambulatory blood pressure monitoring devices (Mobil-O-Graph® NG) used for obtaining the 24h blood pressure values registered blood pressure every 15 minutes during this daytime period (maximum of 48 measurements). Missing data were attributed to technical flaws of the 24h ambulatory blood pressure

monitors, such as movement artefacts or problems with inflating and deflating. Of the 306 patients remaining, the following variables were collected from patient files: Body Mass Index, pulse pressure, whether or not antihypertensive medication was used and whether or not the patient was diabetic. The criterion for hypertension, based on literature, was defined as a daytime (9 a.m. – 9 p.m.) mean blood pressure exceeding either systolic or diastolic pressure by 135 and 85 mm Hg respectively. This criterion was used irrespective of antihypertensive treatment. An additional aspect considered when analysing the 24h ABPM was the diagnosis stated by the cardiologist in the patient files [10].Taking the retrospective study design into account, ethical approval and informed consent were not required. The study complies with the Declaration of Helsinki.

Outcome measures

The main outcome measure in this study is the timing and number of blood pressure measurements one should carry out at home to reliably approximate the 24h average blood pressure. As a secondary finding, the influence of the collected variables on the clinical diagnosis of arterial hypertension was assessed.

Statistical analyses

All statistical analyses have been performed with SAS software version 9.4. Continuous variables were described as mean ± SD. Categorical variables were presented as numbers and percentages. Missing values from the blood pressure measurement were considered missing completely at random and were not implemented in the statistical analyses.

Logistic regression and proportion tests were carried out for a descriptive purpose. Proportion tests have been implemented to compare the clinical diagnosis of hypertension and the diagnosis based on the 24h mean blood pressure criteria mentioned above.

To determine the optimal time of day for measuring blood pressure in the home-setting kappa coefficients were used. Hypertension diagnoses based on 24h ABPM daytime values combined in four-hour intervals were analysed for their correlation with hypertension diagnosis based on the overall daytime blood pressure mean. [11]

Canonical correlations, a measure of associations between two sets of variables, were used to explore the required number of measurements to reliably diagnose hypertension. Calculations have been carried out within the same four-hour time intervals used for kappa coefficients. [12]

Finally, random sampling was conducted within the time interval of interest to select the proposed number of measurements taken within the most predictive time interval in diagnosing arterial hypertension. The diagnosis based on the mean blood pressure within the different samples obtained by random sampling was always compared to the diagnosis based on the mean daytime blood pressure. Specificity, sensitivity, positive and negative predictive values were calculated.

Results

Descriptive statistics

Table 1 lists some characteristics of the 306 patients included in the statistical analyses. 162 (53%) individuals were diagnosed with hypertension according to the criteria mentioned above. 132 of these people (81%) had already been receiving antihypertensive treatment. However, based on the 24 ABPM, 200 (65%) patients were diagnosed with arterial hypertension. The mean 24h blood pressure was 132/79 ± 14/11 mmHg. Mean daytime blood pressure was 143/81 ± 15/12 mmHg.

Logistic regression indicated age ($p = 0{,}0487$), gender ($p < 0{,}0001$) and pulse pressure ($p < 0{,}0001$) to significantly influence the risk of having arterial hypertension at 5% significance level.

Timing and number of measurements

Kappa coefficients in the four-hour time intervals showed a good agreement for all time blocks. However, morning (9 a.m. - 1 p.m.) (κ =0,68) and evening (5 p.m. - 9 p.m.) (κ =0,70) blood pressure measurements had lower kappa values than those taken during the afternoon (1 p.m. - 5 p.m.) (κ =0,78).

As to canonical correlation, having compared the three time intervals with each other, all six charts indicated eight to ten blood pressure measurements are sufficient to diagnose a patient with hypertension. Two charts from analyses with the second and third and the third and first interval respectively are shown (Chart 1 and 2). As can be seen on both charts most of the rise in correlation was achieved before reaching a number of eight to ten blood pressure measurements. Any additional measurements did no longer contribute to a meaningful rise in the correlation between the two sets of blood pressure measurements. .

Random sampling

A simple random sample of 8 measurements out of the 24h ABPM afternoon interval (1p.m. – 5 p.m.) was conducted five times for each patient (table 2). Every set of 8 measurements had an equal chance to be selected. The mean blood pressure based on these 8 measurements was used to diagnose hypertension. This diagnosis was compared to the diagnosis based on the daytime mean blood pressure criteria.

Discussion

Our study shows that blood pressure readings measured between one and five p.m. show the best agreement with an individual's daytime blood pressure average. Furthermore, a maximum of eight to ten home measurements in one afternoon should be sufficient to reliably

approximate an individual's mean daytime blood pressure, with a high sensitivity (86,1 % - 87,8%) and positive predictive value (91,1% - 92 %) .

Home blood pressure measurements vs ambulatory blood pressure measurements

In general, ambulatory blood pressure measurements and home blood pressure measurements correlate better with cardiovascular outcome when compared with office measurements. [5, 8, 13] Mancia et al. showed home blood pressure monitoring (HBPM) as well as 24h ABPM – even daytime records – provide significantly lower blood pressure values than office blood pressure measurements. HBPM values are somewhat higher than those from ABPM, but the difference between their blood pressure averages is negligible. [14]

Verdecchia et al. recommend 24h ABPM in the initial assessment of hypertension in untreated patients. They suggest the use of home blood pressure measurements only for follow-up in treated patients. They state HBPM will not replace 24h ABPM, but rather will complement it. [15] These findings were confirmed by Parati et al. According to their study, HBPM is particularly useful for long-term follow up as it is cheaper than ABPM and may improve adherence to treatment. [9]

Number and timing of measurements

According to canonical correlation analyses, a number of only eight to ten blood pressure measurements should be recorded to reach a high level of accuracy. All of these measurements could be taken within the same day. More specifically, the study results indicate blood pressure should be measured between one and five p.m. The average blood pressure in this afternoon interval had the highest correlation with the daytime average blood pressure. There is little literature supporting nor rejecting the statement about the ideal time of day for recording blood pressure. As mentioned below, the European Society at present

recommends blood pressure measurements should be performed in the morning and evening, but this recommendation is based on little scientific evidence. [16]

Regarding the optimal number of blood pressure measurements, some studies have been carried out. Stergiou et al. investigated the optimal schedule for home blood pressure monitoring. In their research, home blood pressure measurements were taken twice a day, two in the morning and two in the evening, for a period of three days. Stergiou and colleagues concluded an increasing number of readings was consistent with a rise in prognostic power. Although the models with twelve measurements showed the highest prognostic value, a plateau in home blood pressure average and prognostic ability was attained after eight readings. The first blood pressure measurement of each couple was considerably elevated, underscoring the unreliability of a single blood pressure measurement even in the home setting. Blood pressure measurements in the study of Stergiou et al. were collected in the morning (6:30 a.m. – 10:00 a.m.) and evening (5:00 p.m. – 11:00 p.m.). Therefore, the time interval considered best based on our data was excluded. [17] In another study Niirranen et al. concluded seven home measurements may be needed to accurately diagnose arterial hypertension. A single blood pressure measurement however already gave a strong indication concerning cardiovascular events. Niiranen and colleagues stated increasing the frequency of measurements above seven is unnecessary. Besides, it could cause errors in measurements and lower patient compliance. [18]

In a recent study, W-Y. Yang et al. concluded 6 daytime and 2 nighttime blood pressure readings are sufficient in an epidemiological context to estimate an individuals' ambulatory blood pressure without meaningful loss of information. The study also mentioned the discomforts patients can experience when undergoing a 24h ABPM. However, the study results, similar to the results in this article, cannot yet be implemented in clinical practice. (19)

The guidelines from the European society state patients should record their blood pressure four times a day in the home environment. They should take two morning and two evening measurements for at least three days, although a period of seven days is preferred. The mean blood pressure is calculated after omitting the first day's values. According to the guidelines, the obtained average should be a good approximation of the 24h blood pressure mean. [16] Again, blood pressure monitoring in the afternoon is not considered and neither it is in the following studies. The study results from Niiranen et al. also indicate blood pressure measurements in the home-setting should be taken four times a day, two in the morning and two in the evening, for at least three days, but preferably for seven days. However, dropping the blood pressures of the first day for calculating the average would have no additional predictive value according to their study. [19] Verberk et al. propose yet another HBPM scheme. Patients should measure their blood pressure three times in the morning and three times in the evening for seven days. When determining the average blood pressure, values from day one and two should be omitted, as well as the first measurement of each triplet. [7] The random sampling conducted in this study shows 8 measurements chosen at random from the afternoon interval have a high positive and negative predictive value, sensitivity and specificity. These promising results emphasize the need for further research in the diagnosis of arterial hypertension based on self-measurement by patients. This research should include specific cardiovascular outcomes to evaluate the usability of 8 measurements during the afternoon in predicting these outcomes.

Limitations

In this observational study, 24h ABPM readings were analysed to determine the number and timing of blood pressure measurements needed in the home environment to reliably approximate the 24h average blood pressure. [14]

In this retrospective study, we did not include additional variables which could influence the required number and timing of home blood pressure measurements, such as age, gender, medication etc. Future research should therefore comprise distinctive patient characteristics.

Clinical implications

According to our study, a protocol of 8 to 10 blood pressure measurements during the afternoon (1p.m. – 5 p.m.) was found to be trustworthy to accurately diagnose arterial hypertension and could compensate for measuring a whole daytime 24-h ABPM. The assumption was made that when blood pressure mean for a 24h ABPM interval approached the overall daytime blood pressure average, measurements taken within the same time interval in the home environment would also approximate the 24h blood pressure mean. Such a number and time-limited protocol would ease out of office blood pressure measurements. However, before implementing the suggested recording scheme in clinical HBPM practice, it should be tested prospectively in combination with clear cardiovascular outcomes. Furthermore, the possibility of carrying out HBPM during one's work should be assessed respected the European Society of Hypertension guidelines discourage measuring home blood pressure during weekend days. Lastly, future research should determine the ideal dispersion of measurements required to diagnose arterial hypertension.

The Authors declare that there is no conflict of interest

Author contributions

VR, CB, LH, IF and PD contributed to the conception or design of the work. All contributed to the acquisition, analysis, or interpretation of data for the work. VR, CB, IF and PD drafted

the manuscript. All critically revised the manuscript and final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

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Appendix (separate files)

Figure 1: The flowchart illustrates the patient selection for the study population. (*)[10]

Table 1: This table shows the patient characteristics from the study sample.

Table 2: Outcomes from the 5 random samplings

Chart 1: This chart illustrates the correlation between a certain amount of measurements from the second time interval (1 p.m. - 5 p.m.) and all of the measurements from interval three (5 p.m. - 9 p.m.).

Chart 2: This chart illustrates the correlation between a certain amount of measurements from the third time interval (5 p.m. - 9 p.m.) and all of the measurements from interval one (9 a.m. - 1 p.m.).