How many measurements are necessary in diagnosing mild to moderate hypertension?

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Objective. The aim of this study was to investigate how many blood pressure measurements are necessary in diagnosing mild to moderate hypertension.

Methods. The subjects were 99 outpatients who were included on the basis of elevated diastolic (95 ≤ DBP ≤ 115 mmHg) and/or systolic (160 ≤ SBP ≤ 200 mmHg) blood pressure. After the initial measurement all patients underwent nine subsequent blood pressure measurements over a period of 7 months. None of the patients received antihypertensive drug treatment during the study.

Results. Between the first (initial) and second measurements, there was a significant reduction in systolic (161.0 to 152.5 mmHg) and diastolic (101.5 to 97.1 mmHg) blood pressures ($P < 0.01$). The differences between pairs of subsequent measurements were not statistically significant. The average of the last five assessment sessions (two readings per session) was regarded as the ‘conceptual average blood pressure’. Comparing the blood pressure at repeat measurement with the conceptual average blood pressure revealed misclassification in 19\% of cases, even after four repeat measurements (threshold value 95 mmHg). Analysis of the subgroups (95 ≤ DBP < 105 mmHg and 105 ≤ DBP ≤ 115 mmHg) revealed that the proportion of misclassification greatly depended on the initial value and the accepted threshold value. At a threshold value of 95 mmHg, patients with ‘high’ initial diastolic blood pressure (105 ≤ DBP ≤ 115 mmHg) required only two repeat measurements (misclassification in 7\% of cases after four repeat measurements). Of those with initial diastolic blood pressure values between 95 and 105 mmHg, 24\% were misclassified after four repeat measurements.

Conclusions. For these ‘borderline’ diastolic values, we propose larger numbers of measurements than are recommended in international guidelines. Our advice for values in this borderline region is to be reticent in starting antihypertensive drug treatment. The presence or absence of other cardiovascular risk factors should be taken into account when deciding whether treatment is required or not.

Keywords. Blood pressure determination, essential hypertension, general practice, office blood pressure.

Introduction

High blood pressure found incidentally, defined as a blood pressure above a certain level, tends to be lower when it is measured on subsequent occasions.\textsuperscript{1} This can be attributed to the phenomenon of regression towards the mean on the one hand, and to the cuff response effect on the other. Regression towards the mean is a statistical phenomenon: it also occurs, in the opposite direction, with low initial values.\textsuperscript{2} Cuff response is a type of defence reaction, which diminishes on repeating the measurement as the person becomes more familiar with the procedure.\textsuperscript{3}

If there is a large difference between the blood pressure measured and the clinically relevant threshold, the probability of misclassification will be low. Blood pressures near the threshold, in the borderline region between high and low, may easily lead to misclassification.\textsuperscript{4} In view of these phenomena, an important question relates to the number of measurements necessary for a correct diagnosis.

There are no general guidelines with regard to the minimum number of measurements. The guidelines of the WHO/ISH Meeting in 1993 say that if the initial diastolic pressure averages between 90 and 104 mmHg, measurements should be repeated on at least two further occasions during the next 4 weeks.\textsuperscript{5} If the initial

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diastolic values lie between 95 and 105 mmHg, the consensus meeting of Dutch physicians recommended three measurements during the next weeks or months, with three measurements per session. The 1993 Report of the American Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure states that an initial elevated measurement should be confirmed on at least two subsequent visits. The ‘NHG-Standard Hypertension’, a guideline published by the Dutch College of General Practitioners, proposes different numbers of measurements for patients with initial diastolic readings between 105 and 115 mmHg of (three visits) and patients with initial values between 95 and 105 mmHg (five visits). In this guideline, the diagnosis is based on the average of all diastolic readings, with the exception of the initial value. The BHS (British Hypertension Society) recommends that two or more blood pressures should be measured at each visit on up to four separate occasions.

There is no generally accepted threshold level of blood pressure for drug treatment. The BHS guidelines recommend a diastolic threshold of 100 mmHg for drug treatment, whereas others prefer 90 or 95 mmHg. The guideline of the Dutch College of General Practitioners recommends 105 mmHg as the threshold value for drug therapy, unless there are two or more other cardiovascular risk factors.

The objective of the present study was to investigate the number of measurements required for diagnosing mild to moderate hypertension with sufficient certainty. The importance of a correct diagnosis arises from the consequent long-term treatment, including the risks and side effects of potent drugs. Misclassification may inflict unjustified treatment, or may incorrectly withhold treatment. This dilemma is particularly experienced in general practice where the majority of hypertensive patients are diagnosed and many patients have blood pressures which are hovering near the threshold level for treatment.

Patients and methods

Seventeen GPs participated in the study. Participating physicians were given instructions on adequate techniques of blood pressure measurement. Phase V of the Korotkov sound was recorded as the level of diastolic pressure.

Patients were selected for this study on the basis of an initially elevated blood pressure. Inclusion criteria were (i) mean of two systolic values (measured in one visit) between 160 and 200 mmHg and/or mean of two diastolic measurements between 95 and 115 mmHg; and (ii) age between 20 and 75 years. Exclusion criteria were (i) known hypertension or antihypertensive treatment in the year preceding the study; (ii) secondary hypertension; (iii) congestive heart failure or unstable angina; and (iv) pregnancy. After inclusion, nine visits were arranged over the next 7 months. At each visit, the blood pressure was measured twice. Visits 1, 2 and 3 took place during the 4 weeks after inclusion; subsequent visits over the next 6 months.

Blood pressures were measured by the GP in his office with a conventional calibrated mercury sphygmomanometer, provided with a standard-sized cuff (12 × 35 cm).

Analysis

Results are reported as mean ± SD. Differences between the means of two successive readings (systolic and diastolic) were analysed using Student’s paired t-test. The average DBP (diastolic blood pressure) of the five visits (10 blood pressure measurements) during the last 5 months of the study was regarded as the ‘conceptual average blood pressure’, a compromise between the mean value of four measurements used by Armitage et al. as the reference value and the mean of six measurements used by Watson et al.

The study was approved by the ethics review committee of the University Hospital of Maastricht, The Netherlands. All subjects gave written informed consent for participation in the study.

Results

One hundred and fourteen patients were included in the study. Fifteen dropped out (10 men and 5 women, mean initial SBP 164.7 mmHg, mean initial DBP 105.1 mmHg): six patients started antihypertensive drug treatment, one suffered a heart attack and the other eight withdrew because of non-medical reasons. Ninety-nine patients thus completed the study, 49 men and 50 women (mean age 48 years). The mean initial SBP was 161.0 mmHg and the mean DBP 101.5 mmHg. The mean systolic and diastolic values of the initial (l = inclusion/initial) and subsequent (S1, S2, . . . , S9) readings are shown in Figure 1. There was a significant difference between the systolic (8.5 mmHg) and diastolic (4.5 mmHg) readings l and S1 (P < 0.001). The differences between the mean values of the subsequent readings were not statistically significant. As can be seen from Figure 1, the effect of regression had almost disappeared after the second measurement (S1). In patients with initial diastolic values between 105 and 115 mmHg (n = 28) the averages for first and tenth measurements were 171 and 154.5 mmHg (SBP) and 107.7 and 98.3 mmHg (DBP), a systolic fall of 16.5 mmHg and a diastolic fall of 9.4 mmHg. The patients who were included only on the basis of systolic blood pressure (n = 9) showed an even greater regression (170.6 to 152.1 mmHg) between the first and last measurements (Figure 2). If we regard 95 mmHg as the diastolic threshold value for starting drug treatment,
19\% (11\% false-positive, 8\% false-negative) of the patients with initial diastolic blood pressure values between 95 and 115 mmHg (n = 90) would have been misclassified after four repeat measurements. The proportion of misclassifications in this group at threshold values of 100 and 105 mmHg were comparable (Figure 3a). In the patients with initial diastolic values between 95 and 105 mmHg (n = 62) the proportion of misclassifications on all subsequent measurements was lower at higher threshold values. If we use a threshold value of 105 mmHg, the proportion of misclassifications in this study population was low: in this case one single measurement seemed to be sufficient (Figure 3b). At higher initial diastolic values (105 ≤ DBP ≤ 115 mmHg) the misclassifications consist for the greater part of false-positives and the most serious misclassification refers to a threshold value of 105 mmHg (Figure 3c).

All groups with initial diastolic blood pressures near the relevant threshold value showed a considerable proportion of misclassifications, 20–30\%, even after four repeat measurements.

**Discussion**

In the present study we defined the means of 10 measurements made at the last five of a series of 10 visits as the 'conceptual average blood pressure'. Given the enormous variability of blood pressure one might question this as a plausible standard. On the other hand, the numbers of measurements at later points in time should yield a standard that is relatively free of regression towards the mean and of cuff-responding effects.
The effects of ‘regression towards the mean’ and ‘accommodation to the measurement’ were almost entirely restricted to the first and second measurements. After the second measurement, there was a random fluctuation around a mean value. Within each of the three subgroups (initial DBP < 95 mmHg, 95 ≤ initial DBP < 105 mmHg and 105 mmHg ≤ initial DBP ≤ 115 mmHg) there was a strong decline in SBP and DBP between the initial measurement (I) and the final measurement (S9). This is in agreement with the results reported by Millar and Lever. The very small group of patients who were only included on the basis of SBP (n = 9, DBP < 95 mmHg) showed the greatest decline in systolic values over time. This corresponds with the results reported by Van Loo et al. (n = 5999), indicating that isolated systolic hypertension should not be diagnosed too readily.14

Of the studied group of potentially hypertensive patients and the two subgroups studied, 20–30%, depending on the threshold value chosen, were still misclassified after four repeat measurements. This could explain the reduction in blood pressure following...
measurements, using 95, 100 and 105 mmHg as threshold values, was almost 20%. Different patterns were found in the subgroups (95 mmHg ≤ DBP < 105 mmHg and 105 ≤ DBP ≤ 115 mmHg). Figures 1–3 illustrate what can be intuitively grasped: the proportion of misclassifications is low at relatively low initial values and higher threshold values, and the same applies to relatively high initial values and lower threshold values. If, for instance, a GP measures a blood pressure below 105 mmHg at the first consultation, is only interested in the question ‘should I start drug treatment?’, and accepts a threshold of 105 mmHg for this decision, that single blood pressure measurement is sufficient. If he measures a blood pressure between 105 and 115 mmHg and accepts 105 mmHg as the relevant threshold value, he should base his decision on at least three subsequent measurements, thereby reducing the probability of misclassification from 3 in 4 to 1 in 4. The 3 in 4 probability of misclassification after the first measurement is even worse than what a ‘flip coin’ random choice would generate, which highlights the rather misleading phenomenon of ‘being selected’ on the basis of blood pressure measurement on one single occasion.

The answer to the question of how many blood pressure measurements are required for diagnosis depends on the initial blood pressure and the threshold that is considered relevant for the diagnostic decision. If one considers 95 mmHg as the relevant diastolic threshold value in patients with an initial diastolic blood pressure between 105 and 115 mmHg, two repeat measurements appear to be sufficient. Using the same threshold value in patients with initial diastolic values between 95 and 105 mmHg, a 24% misclassification rate should be taken into account, even after four repeat measurements. More measurements are necessary if blood pressure is hovering near a diagnostic threshold value. If the measured blood pressure is far from this threshold, fewer measurements are required for confident classification.17 Like Jackson et al.,17 we recommend that for these borderline values, other cardiovascular risk factors should be taken into account in the decision whether to treat or not. Our results and conclusions support the statement by Reeves in his detailed review: ‘In the future, individualized assessments of absolute risk incorporating other relevant information, such as age, sex, concomitant risk factors, and co-existing target organ damage, along with the patient’s tolerance for risk and history of drug side effects may replace arbitrary cut points in determining when blood pressure elevation becomes treatable.’18 In comparison with their colleagues in internal medicine and specialty practices, GPs have been found to be more cautious in starting antihypertensive drug treatment, and GPs also paid more attention to other cardiovascular risk factors.19 The present study substantiates this approach by GPs.
References


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