Predictors for the white coat effect in general practice patients with suspected and treated hypertension

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SUMMARY

Background: Ambulatory blood pressure monitoring was introduced more than 40 years ago and is accepted as a clinically useful method to evaluate the white coat effect in patients with suspected and established hypertension.

Aim: To study the differences between blood pressure readings taken in the physician's office in the primary healthcare setting, and ambulatory readings, and to find possible predictors.

Design of study: Prospective study.

Setting: Two primary healthcare centres in Norway.

Method: The study included 221 patients, 107 of whom were on antihypertensive treatment, and 114 of whom were under investigation for possible hypertension. Differences between blood pressure readings taken in the physician's office and ambulatory readings were calculated. Independent predictors for the white coat effect were calculated using linear regression analysis.

Results: The difference between blood pressure readings taken in the office and ambulatory readings was 27 mmHg systolic and 11 mmHg diastolic. For the systolic readings, the following factors were independent predictors of the amount of the white coat effect: mean blood pressure, age, history of smoking, family history of cardiovascular disease, and antihypertensive treatment. For the diastolic readings, they were: mean blood pressure, history of smoking, and sex of the patient (with this being most significant for women).

Conclusion: Ambulatory blood pressure measurement is of significant value in identifying patients with white coat hypertension. It can be an important supplement for use in the diagnosis and follow-up of patients with hypertension in general practice.

Keywords: ambulatory blood pressure monitoring; white coat hypertension; hypertension.

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Introduction

UNTIL a few years ago, the only method of screening for hypertension was the measurement of blood pressure by a physician, using a sphygmomanometer, in the physician's office of a primary healthcare facility. One single pressure recording in the office gives, at best, a rough estimate of a person's usual blood pressure,[1] and measurements are often influenced by the interaction between the patient and the physician.[2] It is, therefore, paradoxical that arterial hypertension should be diagnosed on the basis of a few occasional blood pressure measurements, with the consequence that patients may be placed on antihypertensive treatment for the rest of their lives.

Ambulatory blood pressure monitoring was introduced more than 40 years ago, and is now fully accepted as a clinically useful method.[3] These days, ambulatory blood pressure devices are to be found both in hospitals and in numerous general practices in Norway. They are used to diagnose hypertension based on numerous recordings, the advantage being that ambulatory blood pressure readings have lower variability than those taken in the physician's office.[4,5] Many studies have shown that ambulatory blood pressure measurement is a better predictor of organ damage than measurement carried out by physicians.[6-9] In addition, it is used because of the white coat effect, which is defined as a significant fall in blood pressure as measured by ambulatory or home blood pressure measurement, compared with that measured in a clinical setting.[10] If the ambulatory blood pressure reading is normal, compared with an elevated reading in a clinic, the patient has white coat hypertension.[3,10] The proportion of hypertensive patients with white coat hypertension has been estimated to be between 15% and 30%.[3]

The 1999 World Health Organisation/International Society for Hypertension (WHO/ISH) Guidelines for the Management of Hypertension emphasise that the decision to treat a patient with hypertension 'is not based on the level of blood pressure alone but on assessment of the total cardiovascular risk in that individual'.[11] Until now, risk calculations have been based on blood pressure readings taken in the physician's office, and no valid calculations have been made using ambulatory blood pressure values.[12] The introduction of ambulatory blood pressure measurement in general practice may have an impact on physicians' decisions as to whether to treat patients with antihypertensive drugs or not. It has not been clarified which patients should have ambulatory blood pressure measurement before starting antihypertensive treatment. The objective of this paper is to study the magnitude of the white coat effect, and to evaluate predictors for the size of it.

HOW THIS FITS IN

What do we know?

In hypertensive general practice patients, 15–30% have white coat hypertension.

What does this study add?

The white coat effect demonstrated was large: 27 mmHg systolic and 11 mmHg diastolic. The following factors were independent predictors for the size of the white coat effect for systolic readings: mean blood pressure, age, smoking, family history of cardiovascular disease and antihypertensive treatment. For diastolic readings they were: mean blood pressure, smoking and sex (women highest).

Method

A prospective study was performed at two Norwegian health centres between August 1998 and December 1999. Patients who were selected were divided into two groups: those who were receiving treatment for hypertension, and those who were under investigation for possible hypertension.

The inclusion criteria were: systolic blood pressure greater than the number of years of the patient's age plus 100 mmHg, and/or elevated diastolic pressure, including the following: age under 40 years and a diastolic pressure of more than 90 mmHg; age between 40 and 59 years, with a diastolic pressure of more than 95 mmHg; age between 60 and 79 years, with a diastolic pressure of more than 100 mmHg.

Exclusion criteria were: age 80 years and above, established secondary hypertension, known alcoholism or drug abuse, established moderate to serious heart failure or kidney failure, known aortic aneurysm, blindness or deafness, and systolic blood pressure above 220 mmHg or diastolic pressure above 125 mmHg.

The patients underwent at least two blood pressure controls, with an interval of at least 2 weeks before entering the study, following the national guidelines for measurement.[10] They were included in the study if one of the blood pressure readings taken at a visit was above the given limits. Mean systolic and diastolic pressures were calculated based on these two measurements. A 24-hour ambulatory blood pressure measurement was taken on all of the patients using a Mobil-O-Graph device, and mean daytime systolic and diastolic pressures were collected. White coat hypertension was defined as a mean daytime reading of less than 135 mmHg systolic and less than 85 mmHg diastolic.[13] The differences between the office systolic and diastolic pressures and the mean ambulatory daytime pressures were calculated.

A cardiovascular risk score was then calculated using the office blood pressure readings. This was based on the data from the Framingham study.[12] The calculation was based on office blood pressure readings, the presence of diabetes mellitus, the total cholesterol and high density lipoprotein (HDL) values, smoking, age and sex, and family history of cardiovascular disease. A cut-off of more than 20% was used for intervention of risk of cardiovascular disease in the next 10 years. Using the mean daytime reading would have meant that the risk calculation would have been underestimated, since the Framingham calculations are based on blood pressure readings taken in the clinic.

In the statistical analysis, proportions were analysed using χ^2 statistics, and means by using the Student's *t*-test. A linear regression analysis, with differences between the mean daytime ambulatory blood pressure and office blood pressure readings as dependent variables, was performed using the general linear model in SPSS 8.0. Variables with a bivariate association of $P<0.20$ were included, and a backwards selection was performed. Owing to mathematical considerations, ambulatory and office blood pressure readings could not be included in the calculations as independent variables, so the mean of the office systolic and diastolic pressures was included as an independent variable. The level of significance was 0.05.

Results

Two hundred and twenty-one patients were recruited. In the group undergoing investigation ($n = 114$) the mean age was 55.8 years (standard deviation [SD] = 10.1), and 62 (54%) were males. In the group of patients with hypertension ($n = 107$) the mean age was 60.3 years (SD = 10.5) and 54 (51%) were males.

In the group undergoing investigation, the following blood pressure readings were recorded: office blood pressure readings showed a mean systolic of 172.7 mmHg (95% confidence interval [CI] = 169.1 to 176.3) and a mean diastolic of 100.6 mmHg (95% CI = 99.2 to 102), while ambulatory pressures showed a mean systolic of 147.3 mmHg (95% CI = 144.4 to 150.2) and a mean diastolic reading of 89.7 mmHg (95% CI = 87.7 to 91.7), giving mean differences of 25.3 mmHg systolic and 10.8 mmHg diastolic, respectively.

In the group of patients with hypertension, the following blood pressures were recorded: office blood pressures showed a mean systolic of 169.6 mmHg (95% CI = 166 to 173.2) and a mean diastolic of 96.4 mmHg (95% CI = 94.8 to 98), while ambulatory pressure readings showed a mean systolic of 141.1 mmHg (95% CI = 138.3 to 143.9) and a mean diastolic of 85.6 mmHg (95% CI = 83.6 to 87.6), giving a mean difference of 28.6 mmHg systolic and 10.8 mmHg diastolic (Table 1). In the group undergoing investigation, 18 (16%) patients had white coat hypertension. Similarly, 28 (27%) of the patients in the group with hypertension had significant white coat hypertension, giving a total of 46 patients with mean daytime ambulatory blood pressure readings of less than 135/85 mmHg.

One hundred and sixty-six patients (75%) had a difference in systolic measurement of 15 mmHg or more, and 52% had a difference in diastolic measurement of 10 mmHg or more. Fifteen per cent of all the patients had a diastolic ambulatory blood pressure reading higher than that taken in the office.

In the calculation of the risk for cardiovascular disease in the next 10 years, 54 (31%) of the 176 patients included had a risk higher than 20%.

Tables 2 and 3 show the results of a multiple linear regression analysis of independent factors predicting the magnitude of difference between systolic and diastolic ambulatory blood pressure (mean daytime pressure) and office blood pressure readings. The following factors were found to be significant with regard to the systolic difference: mean blood pressure, age, smoking, family history of cardiovascular disease, and

Table 1. Mean daytime office and ambulatory blood pressure readings and differences between readings in two groups of patients from two Norwegian primary healthcare centres.[a]

	Group with hypertension (*n* = 107)		Group receiving investigations (*n* = 114)		Total (*n* = 221)	
	Office	Ambulatory	Office	Ambulatory	Office	Ambulatory
Mean systolic blood pressure in mmHg (95% CI)	169.6 (166.0 to 173.2)	141.1 (138.3 to 143.9)	172.7 (169.1 to 176.3)	147.3 (144.4 to 150.2)	171.2 (168.6 to 173.8)	144.3 (142.2 to 146.3)
Mean difference (95% CI)	28.6 (25.2 to 32.00)		25.3 (22.2 to 28.4)		26.9 (24.6 to 29.2)	
Mean diastolic blood pressure in mmHg (95% CI)	96.4 (94.8 to 98.00)	85.6 (83.6 to 87.6)	100.6 (99.2 to 102.00)	89.7 (87.7 to 91.7)	98.5 (97.4 to 99.6)	87.7 (86.3 to 89.2)
Mean difference (95% CI)	10.8 (8.8 to 12.8)		10.8 (8.8 to 12.8)		10.8 (8.8 to 12.8)	

[a]One group had established hypertension and one was under investigation for hypertension.

Table 2. Linear regression analysis of predictors for the differences between office and ambulatory systolic blood pressure readings.[a]

Variable	Systolic difference[b]				
	Crude *P*-value	*B* in bivariate analysis (95% CI)	Adjusted *P*-value	White-coat hypertension trend in model	*B* in final model (95% CI)
Mean blood pressure (per mmHg)	<0.0001	0.42 (0.33 to 0.50)	<0.0001	Increased	0.37 (0.28 to 0.46)
Age (per year)	<0.00001	0.74 (0.54 to 0.93)	<0.0001	Increased	0.36 (0.17 to 0.55)
Smoking	0.02	6.32 (1.00 to 11.65)	0.008	Reduced	5.69 (1.51 to 9.87)
Family history of cardiovascular disease	0.011	5.81 (1.33 to 10.29)	0.014	Reduced	4.45 (0.90 to 7.99)
Antihypertensive treatment	0.14	3.23 (-1.30 to 7.76)	0.03	Reduced	4.11 (0.41 to 7.81)
Sex	0.02	5.22 (0.71 to 9.74)	0.40		
Absolute risk of cardiovascular disease (per %)	0.04	0.35 (0.11 to 0.58)	0.99		
Doctor	0.02		0.33		

[a]Using the General Linear Model in SPSS 8.0. Variables that were significant with a *P*-value <0.20 in the bivariate analysis were included. [b]R^2 = 0.42 for the final model.

Table 3. Linear regression analysis of predictors for the difference between ambulatory and office diastolic blood pressure readings.[a]

Variable	Diastolic difference[b]				
	Crude *P*-value	*B* in bivariate analysis (95% CI)	Adjusted *P*-value	White-coat hypertension trend in model	*B* in final model (95% CI)
Sex	<0.0001	6.24 (3.62 to 8.84)	<0.0001	Highest in women	5.55 (2.95 to 8.15)
Smoking	0.004	4.68 (1.49 to 7.87)	0.011	Reduced	3.97 (0.91 to 7.03)
Mean blood pressure (per mmHg)	0.02	0.07 (0.01 to 0.14)	0.037	Increased	0.06 (0.04 to 0.12)
Absolute risk of cardiovascular disease (per %)	0.003	0.22 (0.07 to 0.36)	0.34		
Doctor	0.045	0.22 (0.07 to 0.36)	0.11		

[a]Using the General Linear Model in SPSS 8.0. Variables that were significant with a *P*-value <0.20 in the bivariate analysis were included. [b]R^2 = 0.13 for the final model.

antihypertensive treatment. With regard to the diastolic difference, mean blood pressure, smoking, and sex were significantly associated. The explained variance was 0.42% for the systolic difference and 0.13% for the diastolic difference. In the bivariate analysis, the size of *B* expresses the change in difference, with a change of one in the independent variable, all other variables being equal. Therefore, a rise in mean blood pressure of 10 mmHg would give a rise in difference of 3.7 mmHg. Likewise, a rise in age of 10 years would give a rise in difference of 3.6 mmHg.

Discussion

White coat hypertension

In this study, 46 (19.9%) out of 221 patients had white coat hypertension. The inclusion criteria were conservative in order to avoid patients with borderline blood pressure, so that the proportion of patients with white coat hypertension should not be overestimated. The difference between office and ambulatory readings is also surprisingly high. In the PAMELA Study, the researchers found a difference of 8.2 mmHg in systolic blood pressure.[14] The difference, however, depends on

where the blood pressure is on the scale. Verdecchia *et al* showed that patients with a high average of 173 mmHg systolic in the clinic had an average ambulatory daytime blood pressure reading of 135 mmHg.[15] The present study had a rather high inclusion blood pressure, and is therefore comparable with the findings of Verdecchia. Other studies have also found differences of the same magnitude.[16,17]

In a recent review article, it was postulated that patients with white coat hypertension are characterised by the following: absence of organ damage induced by hypertension; absence of risk of future cardiovascular disease related to hypertension; and absence of lowering of blood pressure from antihypertensive treatment.[13]

The authors conclude that current evidence strongly indicates that patients with white coat hypertension have a lower risk of target organ damage than patients with persisting hypertension. The definition of white coat hypertension is still debated. The authors claim that the mean daytime blood pressure should be less than 135/85 mmHg, which we used in this study, while others use 140/90 mmHg as the limit of white coat hypertension.

In the 1999 WHO/ISH Guidelines for the Management of Hypertension, it is emphasised that the decision to treat a patient with hypertension 'is not based on the level of blood pressure alone but on assessment of the total cardiovascular risk in that individual'.[11] It is a problem that, until now, office blood pressure readings have been used in the risk calculations, and no valid calculations have been based on ambulatory blood pressure values.[12]

In our study the following factors were found to be significant with regard to the systolic difference: mean blood pressure, age, smoking, family history of cardiovascular disease, and antihypertensive treatment. With regard to the diastolic difference, mean blood pressure, smoking, and sex were significantly associated. These findings can be used to single out patients with a higher chance of having white coat hypertension, and they should have ambulatory blood pressure readings performed before a decision is made to start or change antihypertensive treatment.

It would appear that the conclusion to be drawn from our study would be that a mean difference should be subtracted from the office blood pressure to find a presumed ambulatory blood pressure, and that a treatment decision should be based on this, but we would not recommend this practice. Previous studies have demonstrated that individual profiles vary greatly with regard to the white coat effect, and the amount of variation in the individual patient can be hard to predict. General practitioners should probably make greater use of ambulatory blood pressure monitoring in the diagnosis and follow-up of hypertensive patients.

Implications for further research

It is important that new data are developed to calculate the risk for patients in which ambulatory blood pressure readings are included. Using this data will enable us to predict with higher accuracy which patients are at risk and in need of treatment. Furthermore, the use of ambulatory blood pressure measurement will help us to single out patients with white coat hypertension who are not in need of antihypertensive treatment.

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