Is “Isolated Home” Hypertension as Opposed to “Isolated Office” Hypertension a Sign of Greater Cardiovascular Risk?

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Background: The SHEAF (Self-Measurement of Blood Pressure at Home in the Elderly: Assessment and Follow-up) study is an observational study (from February 1998 to early 2002) designed to determine whether home blood pressure (BP) measurement has a greater cardiovascular prognostic value than office BP measurement among elderly (≥60 years) French patients with hypertension. The objective of this present work is to describe the baseline characteristics of the treated patients in the SHEAF study from February 1998 to March 1999, placing special emphasis on “isolated office” and “isolated home” hypertension.

Methods: Baseline office BP measurement was assessed using a mercury sphygmomanometer. Home BP measurement was performed over a 4-day period. A 140/90–mm Hg threshold was chosen to define office hypertension, and a 135/85–mm Hg threshold to define home hypertension.

Results: Of the 5211 hypertensive patients in the SHEAF study with a valid home BP measurement, 4939 received treatment with at least 1 antihypertensive drug. Patients with isolated office hypertension represented 12.5% of this population, while patients with isolated home hypertension represented 10.8%. The characteristics of the patients with isolated office hypertension were similar to those of patients with controlled hypertension. However, patients with isolated office hypertension had fewer previous cardiovascular complications. In contrast, rates of cardiovascular risk factors and history of cardiovascular disease in patients with isolated home hypertension resembled those in patients with uncontrolled hypertension.

Conclusions: This retrospective analysis suggests that patients with isolated home hypertension belong to a high-risk subgroup. The 3-year follow-up of these patients will provide prospective data about the cardiovascular prognosis of these subgroups.

Arch Intern Med. 2001;161:2205-2211

Hypertension is one of the most prominent risk factors for cardiovascular disease in industrialized countries. Cardiovascular morbidity and mortality remain high in spite of the many drug therapies and treatment guidelines for hypertension as well as the appropriately designed controlled trials and meta-analyses providing precise evaluations of the potential benefits of treatment. There are probably many explanations for this, from inappropriate diagnosis to inappropriate management. The primary step in hypertension management is blood pressure (BP) measurement. Until now, the clinical gold standard for measuring BP was with a sphygmomanometer at a physician’s office. Epidemiological studies have established the prognostic value of BP measured by conventional methods. Moreover, therapeutic trials using the conventional method for measuring BP have shown that a reduction in BP is associated with a reduction in cardiovascular morbidity and mortality. However, for many years it has been shown that measurement by physicians lacks exactitude (digital preference) and reproducibility. Conversely, quality of both automatic devices (used for ambulatory and home measurements) and their validation is now acceptable. Using these methods, physicians have shown that in some patients office BP is persistently elevated whereas BP outside the clinical environment (at home or in ambulatory conditions) is not. This condition is widely known as “white coat” hypertension, although the term isolated office hypertension is now preferred. Controversy remains on whether isolated office hypertension is a benign clinical condition or is linked with an increased risk of target organ damage and a worse prognosis.

The converse phenomenon “reverse white coat effect” or “white coat normotension” has already been discussed. Although few data are available, they support the hypothesis that subjects with these conditions may represent a high-risk group.
PATIENTS AND METHODS

DESIGN AND PATIENTS

The SHEAF study is a 3-year prospective cohort study designed to assess whether the prognostic value of home BP measurement is greater than that of office BP measurement. Subjects of both sexes were recruited by general practitioners and included when they fulfilled the following inclusion criteria: (1) 60 years or older; (2) primary permanent hypertension defined by the presence of an antihypertensive treatment or, in the absence of treatment, by an office BP higher than 140/90 mm Hg on 2 separate occasions during the prior year; (3) arm size allowing the use of a standard cuff; (4) ability to perform an appropriate number of BP measurements at home with the device of the study (the Omron HEM-705-CP device; Omron Corporation, Tokyo, Japan); and (5) absence of any threatening disease or recent acute cardiovascular events (eg, myocardial infarction or stroke).

The study comprised 2 successive phases. The first phase consisted of a 2-week period of evaluation with 2 separate visits performed 2 weeks apart. Medical history of the patients and antihypertensive treatments were recorded as well as office and home BP measurements. This phase took place from February 1998 to March 1999. The second phase was a 3-year follow-up of patients. Follow-up visits are to be performed every year by the patients' general practitioners. There is no specific recommendation with regard to management of hypertension and BP goals. The primary end point is cardiovascular mortality. Secondary end points are total mortality and the combination of cardiovascular mortality, myocardial infarction, stroke, transient ischemic attack, hospitalization for angina or heart failure, percutaneous transluminal coronary angioplasty, or coronary artery bypass graft. This phase will end in early 2002.

BP MEASUREMENTS

Office BP Measurement

During the first phase, triplicate BP measurements were taken at each visit by the physician using a mercury sphygmomanometer with the patient in the sitting position after a 3-minute rest. No recommendation about time of measurement was made to the physicians. Systolic BP was measured at phase 1 of the Korotkoff sounds and diastolic BP at phase 5 of the Korotkoff sounds. The mean of the 6 readings was considered the office baseline BP measurement for each patient.

Home BP Measurement

Home BP measurement was performed during the first phase of the study. It was planned over a 4-day period chosen at the patient’s convenience. Every day a series of 3 consecutive measurements was requested in the morning (8 AM) and repeated in the evening (8 PM). Measurements were performed with the patient in the sitting position after a 5-minute rest. All subjects used the Omron HEM-705-CP device, which is a printer-equipped, semiautomatic, digitized device based on the oscillometric method. This device had been previously validated by comparison with the mercury sphygmomanometer according to the revised protocol of the British Hypertension Society. Because it has been shown that the degree of reliability of hypertensive patients’ reporting of self-measured BP was both variable and unpredictable, each patient was asked first to write results of measurements in a booklet designed for the study and second, to store all printouts.

Home BP Data Management

For each patient, aberrant BP measurements were deleted according to the following rules: diastolic BP lower than 40 mm Hg or diastolic BP higher than 150 mm Hg; systolic BP lower than 60 mm Hg or higher than 250 mm Hg; and pulse pressure lower than 10 mm Hg. Measurements performed outside the predefined morning and evening times (outside the 4 AM to noon range or the 4 PM to midnight range) were also discarded.

Patients were included in the study only if they exhibited at least 15 valid measurements, with at least 6 measurements in the morning and 6 measurements in the evening. As recommended by the first international...
Differences Between Office and Home BP Measurements: Statistical Approach

For each patient the difference between office and home BP measurements was calculated. For the study population, BP differences were expressed as mean ± SD because they were normally distributed. According to the distribution of the differences, patients were classified into 3 groups: (1) Group A, the “small difference group” included patients whose difference in BP measurements (office minus home) fell within the mean ± SD BP difference of the study population. In these patients, office and home BP measurements were reasonably close. (2) Group B included patients with differences in BP measurements greater than 1 SD above the mean. These patients presented with an office BP measurement higher than a home BP measurement. This refers to the commonly labeled “white coat effect” or “office effect.” (3) Group C included patients having a difference in BP measurement lower than 1 SD below the mean. These patients presented with a home BP measurement higher than an office BP measurement. This group was labeled with “home effect” as opposed to office effect. This analysis was performed for systolic BP, diastolic BP, and pulse pressure, and only in patients treated with antihypertensives drugs.

Differences Between Office and Home BP Measurements: Clinical Approach

In this approach we used cutoff points to compare the 2 methods to obtain a 2 × 2 table in which a patient belonged to 1 of the 4 following categories: (1) normal BP by the 2 methods (controlled hypertension); (2) high BP by the 2 methods (uncontrolled hypertension); (3) high BP with office BP measurement and normal BP with home BP measurement (commonly called isolated office hypertension); and (4) normal BP with office BP measurement and high BP with home BP measurement (which we propose to call “isolated home hypertension”).

Because patients were already treated in this analysis, we chose 140/90 mm Hg as the threshold for the office BP measurement, which refers to the officially recommended goal for antihypertensive treatment. According to the first international consensus conference of self-BP monitoring, the threshold defining hypertension on the basis of home BP measurement was 135/85 mm Hg.

Statistical Analysis

Quantitative data are summarized as mean ± SD and qualitative data as percentages. The normality of distributions was verified using the Kolmogorov-Smirnov test. Linear correlations between office and home BP measurements were calculated using the Pearson coefficient. Comparisons among the 3 groups defined in the “Statistical Approach” section and comparisons among the 4 groups defined in the “Clinical Approach” section were performed as follows: (1) For quantitative variables (eg, BP, heart rate, and age) the between-group comparisons were performed using a 1-way analysis of variance. (2) For qualitative variables (eg, cardiovascular risk factors and history of cardiovascular diseases), the between-group comparisons were performed using the χ² test. (3) When age could explain between-group differences, a covariance analysis was performed. (4) With 3 groups of patients in the statistical approach and 4 groups of patients in the clinical approach, multiple comparisons concerned 3 and 6 pairs of means, respectively, for each variable. Because multiple comparisons were not planned in the protocol, we chose to remain descriptive. P < .05 was considered statistically significant. However, because of the large number of patients recruited in this study, the power was very high and, consequently, small differences between groups could be statistically significant. Therefore, in addition to statistical significance, between-group differences should also be analyzed with reference to their clinical significance. All calculations were performed using SAS version 6.12 statistical software (SAS Institute Inc, Cary, NC).

A linear correlation was found between office and home BP measurements for both systolic BP (r = 0.62; P < .001) and diastolic BP (r = 0.54; P < .001). According to this regression line, the self-recorded BP equivalent to a conventional pressure of 140 mm Hg (systolic) and 90 mm Hg (diastolic) was 138/85 mm Hg, and thus the 135/85 mm Hg threshold proposed by the first international consensus conference of self-BP monitoring was confirmed.

Differences Between Office and Home BP Measurements: Statistical Approach

Home BP measurement was lower than office BP measurement by 5.9 ± 15.6 mm Hg for systolic BP, 2.6 ± 9.0 mm Hg for diastolic BP, and 3.3 ± 12.0 mm Hg for pulse pressure (all P < .05). These differences held constant whatever the BP level was.

For systolic BP, the reference group (group A) was constituted of patients having a mean difference (office minus home) ranging from –9.7 mm Hg to 21.4 mm Hg. This group comprised 3549 subjects (71.9%). Group B comprised 720 subjects (14.6%). For these patients having a higher BP at the office, the difference between office and home BP measurements ranged from 21.4 mm Hg to 102.0 mm Hg. Group C comprised 670 subjects (13.6%). For these patients having a higher BP at home, the difference between office and home BP measurements ranged from –9.7 mm Hg to –72.6 mm Hg.

The characteristics of the 3 groups are given in Table 2. Patients with home effect (group C) had more cardiovascular risk factors: they were older, more often male, more often had diabetes, and more likely to be former smokers. They also were more likely to have a history of cardiovascular disease than subjects in the reference group. Conversely, patients with office effect (group B) were not more likely to have a history of cardiovascular disease than the reference group. These trends were also found in a sex subgroup analysis.
The same trends were observed for cardiovascular risk factors and cardiovascular history between patients with home effect and the reference group when the analysis was performed on pulse pressure. On the other hand, the between-group differences for diastolic BP were only significant for sex and history of stroke (data not shown).

**DISCREPANCIES BETWEEN OFFICE AND HOME BP MEASUREMENTS: CLINICAL APPROACH**

Classification of patients in the 4 groups defined by our cutoffs (140/90 mm Hg for office BP measurement and 135/85 mm Hg for home BP measurement) is given in Table 3. The level of agreement between the 2 methods assessed by the κ statistic was 0.40. Using the conventional threshold, 74% of the patients had systolic BPs over 140 mm Hg or diastolic BPs over 90 mm Hg. Patients with isolated office hypertension represented 12.5% of the population, while patients with isolated home hypertension represented 10.8% of the population. The characteristics of the patients according to the classifications controlled hypertension (both office and home BP measurement), uncontrolled hypertension (both office and home BP measurement), isolated office hypertension, and isolated home hypertension are reported in Table 4. The characteristics of the patients with isolated office hypertension were similar to those with controlled hypertension. However, patients with isolated office hypertension had fewer previous cardiovascular complications (coronary artery disease, 8.4% vs 12.7%);
stroke, 2.8% vs 3.8%). In contrast, patients with isolated home hypertension resembled the patients with uncontrolled hypertension in rates of cardiovascular risk factors and history of cardiovascular disease (coronary artery disease, 13.4% vs 13.1%; history of stroke, 6.8% vs 5.0%). These trends were also found in a sex subgroup analysis (data not shown).

The objective of the SHEAF study is to assess whether home BP measurement has a greater prognostic value than office BP measurement. Until now, 1 study has investigated the prognostic significance of home BP measurement and found that home BP measurement had a stronger predictive power for mortality than did casual BP measurement. However, only 52 cardiovascular deaths were reported in this study, and the greater prognostic value was found for systolic BP but not diastolic BP. Moreover, these results were obtained in a population of mainly normotensive Japanese people, who are known for having different risk of stroke and coronary disease than white populations. The SHEAF study, in which 5211 patients with valid home BP measurements have been included, will allow a more detailed analysis because a larger number of cardiovascular deaths is expected and morbidity data will be available.

As is usually reported, in this work we found lower BPs by home BP measurement than by physician measurements. When using the cutoff point of 140/90 mm Hg for office BP measurement, we found the corresponding point-estimate of home BP to be 138/85 mm Hg. This figure can be compared with the 134/86 mm Hg cutoff found in the Self-Measurement for the Assessment of the Response to Trandolapril (SMART) study, which included 1710 patients with hypertension. It is also in agreement with the first international consensus conference of self-BP monitoring.

Although a correlation was found in this study between the 2 methods, important individual discrepancies are clearly shown. In some patients, BPs measured by the 2 methods were very different, and it was of interest to ascertain whether these differences in BP measurements were associated with differences in demographic and cardiovascular profile of the patients.

To evaluate the differences in BP measurements between the 2 methods, 2 different approaches were used in this work. The first approach, called the statistical approach, is based on the statistical distribution of the differences and does not easily allow for BP management

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**Table 3. Classification of the Patients According to Their Office and Home BP Measurements**

<table>
<thead>
<tr>
<th>Home BP</th>
<th>Office BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controlled Hypertension ≤135 mm Hg (systolic) and ≤85 mm Hg (diastolic)</td>
<td>732 (14.8)</td>
</tr>
<tr>
<td>Uncontrolled Hypertension &gt;135 mm Hg (systolic) or &gt;85 mm Hg (diastolic)</td>
<td>532 (10.8)</td>
</tr>
</tbody>
</table>

**Table 4. Comparison of the Patients According to Their Hypertension Status**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Isolated Home Hypertension (n = 532)</th>
<th>Uncontrolled Hypertension (n = 3058)</th>
<th>Isolated Office Hypertension (n = 617)</th>
<th>Controlled Hypertension (n = 732)</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office SBP/DBP, mm Hg</td>
<td>134 (5)/79 (6)</td>
<td>160 (14)/87 (8)</td>
<td>151 (10)/85 (7)</td>
<td>131 (7)/77 (6)</td>
<td>&lt;.001 &lt;.001</td>
</tr>
<tr>
<td>Office HR, bpm</td>
<td>70 (8)</td>
<td>72 (8)</td>
<td>72 (8)</td>
<td>70 (8)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Home SBP/DBP, mm Hg</td>
<td>144 (10)/83 (7)</td>
<td>156 (5)/86 (9)</td>
<td>127 (6)/74 (6)</td>
<td>123 (8)/74 (6)</td>
<td>&lt;.001 &lt;.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>69.8 (6.5)</td>
<td>70.5 (6.6)</td>
<td>69.4 (6.3)</td>
<td>68.8 (6.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hypertension duration, y</td>
<td>11.3 (7.3)</td>
<td>11.5 (8.6)</td>
<td>10.8 (7.7)</td>
<td>10.8 (7.4)</td>
<td>.051</td>
</tr>
<tr>
<td>Male</td>
<td>57.7</td>
<td>52.2</td>
<td>36.3</td>
<td>38.9</td>
<td>.001</td>
</tr>
<tr>
<td>BMI (&gt;30 kg/m²)</td>
<td>19.1</td>
<td>20.4</td>
<td>15.8</td>
<td>16.2</td>
<td>.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>14.3</td>
<td>15.9</td>
<td>13.3</td>
<td>11.2</td>
<td>.01</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>44.7</td>
<td>43.2</td>
<td>44.6</td>
<td>44.4</td>
<td>.84</td>
</tr>
<tr>
<td>Active smokers</td>
<td>8.3</td>
<td>8.0</td>
<td>6.3</td>
<td>7.2</td>
<td>.49</td>
</tr>
<tr>
<td>Former smokers</td>
<td>26.7</td>
<td>26.4</td>
<td>17.3</td>
<td>20.4</td>
<td>.001</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>13.4</td>
<td>13.1</td>
<td>8.4</td>
<td>12.7</td>
<td>.01</td>
</tr>
<tr>
<td>Heart failure</td>
<td>4.9</td>
<td>5.4</td>
<td>3.6</td>
<td>5.7</td>
<td>.26</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>5.5</td>
<td>7.0</td>
<td>4.1</td>
<td>3.8</td>
<td>.001</td>
</tr>
<tr>
<td>History of stroke</td>
<td>6.8</td>
<td>5.0</td>
<td>2.8</td>
<td>3.8</td>
<td>.01</td>
</tr>
</tbody>
</table>

*Data are number (percentage) of patients. BP indicates blood pressure.

†P values correspond either to 1-way analysis of variance (quantitative variables) or to χ² test (qualitative variables).

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as far as diagnosis or therapeutic decisions are concerned. Indeed, patients presenting with a large between-method difference in BP measurements may exhibit both normal and abnormal BP measurements with the 2 methods. So, we proposed a second approach called the clinical approach, which is based on the classification of patients as normotensive and hypertensive according to predefined cutoff points. This allowed first for the identification of patients with isolated office hypertension, and second, for the identification of patients with isolated home hypertension.

In the present study, using the threshold of 135/85 mm Hg, we found isolated office hypertension in only 12% of the population. This figure is lower than the findings of other studies that report a 20% to 25% prevalence of isolated office hypertension. The definition of the cutoff point may be responsible for the between-study discrepancies. Because the upper limit of normal ambulatory or home BP has been regarded as 140/90 mm Hg in some studies, isolated office hypertension has been reported in a large fraction of the population. The effect of age on white coat hypertension seems to be somewhat conflicting. It has been reported that older patients exhibited white coat hypertension more often than younger patients; however, in the present study, as in some other studies, there was no relation between the presence of isolated office hypertension and age. This may be explained by the fact that all the patients in our study were in the same age range. Consistent with the findings of other studies, we found that patients with isolated office hypertension were more frequently women and were more likely to exhibit the same cardiovascular profile as normotensive patients.

Isolated home hypertension was present in 11% of the population of this study. This figure is higher than the finding of a previous study conducted in patients receiving a recent diagnosis of hypertension, which reported only a 3% prevalence. In addition, the patients with isolated home hypertension represented 42% of the office normotensive patients, whereas only 21% of clinically normotensive patients presented an elevated ambulatory BP in the study of Liu et al.

Using the statistical approach, differences in BP measurements were associated with differences in patients' cardiovascular history. There was a continuous trend across the 3 subgroups for a decrease in risk: patients with office effect exhibited the lowest risk profile, whereas patients with home effect presented the highest prevalence of both risk factors and prior cardiovascular events. Whether these different profiles are linked to different prognoses remains mostly unknown. It has been shown in the prospective Japanese study that office effect was not significantly related to cardiovascular mortality, while the reversed white coat effect, which is equivalent to our home effect, was a strong predictor of cardiovascular risk.

Using the clinical approach, we found that differences in BP measurements were also associated with differences in patient characteristics. Isolated office hypertension was not associated with more frequent previous cardiovascular complications. The prospective follow-up of these patients will address this issue. In already published studies, it has been shown that isolated office hypertension was associated with low cardiovascular risk.

Patients with home hypertension in our study were characterized by a cardiovascular profile similar to the cardiovascular profile of patients with uncontrolled hypertension: they were mainly men and exhibited a high rate of risk factors and previous cardiovascular complications such as history of coronary disease, stroke, or diabetes. These data are close to those previously published in which patients with isolated ambulatory hypertension were older and had higher body mass indexes and glucose levels than normotensive patients. Moreover, this condition was associated with prognostically important target organ damage resulting in increased left ventricular mass and carotid wall thickness when compared with normotensive patients. This supports the hypothesis that patients with isolated home hypertension could represent a high-risk group. Thus, it would be of interest, as it has not been addressed, to determine whether isolated home hypertension is associated with an elevated rate of cardiovascular events. The prospective follow-up of these patients would address this issue.

The prospective SHEAF study included 5211 elderly hypertensive patients. The use of both office BP and home BP measurements allowed us to identify 12% of patients with isolated office hypertension and 11% of patients with isolated home hypertension. The cardiovascular risk profile of these groups was markedly different. The 3-year follow-up will provide a precise evaluation of the cardiovascular prognosis of such patients and assess the concept of isolated home hypertension.

Accepted for publication March 29, 2001.
The authors gratefully acknowledge Prof Joël Ménard, MD, for his comments on this work.
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REFERENCES


