Office, Home, and Ambulatory Blood Pressures as Predictors of Cardiovascular Risk

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Abstract—Ambulatory blood pressure (BP) is considered as the gold standard of BP measurement although it has not been shown to be more strongly associated with cardiovascular risk than is home BP. Our objective was to compare the prognostic value of office, home, and ambulatory BP for cardiovascular risk in 502 participants examined in 1992 to 1996. The end point was a composite of cardiovascular mortality, myocardial infarction, stroke, heart failure hospitalization, and coronary intervention. We assessed the prognostic value of each BP in multivariable-adjusted Cox models. The likelihood χ^2 ratio value was used to test whether the addition of a BP variable improved the model's goodness of fit. After a follow-up of 16.1±3.9 years, 70 participants (13.9%) had experienced ≥1 cardiovascular event. Office (systolic/diastolic hazard ratio per 1/1 mm Hg increase in BP, 1.024/1.018; systolic/diastolic 95% confidence interval, 1.009–1.040/0.994–1.043), home (hazard ratio, 1.029/1.028; 95% confidence interval, 1.013–1.045/1.005–1.052), and 24-hour ambulatory BP (hazard ratio, 1.033/1.049; 95% confidence interval, 1.019–1.047/1.023–1.077) were predictive of cardiovascular events. When all 3 BP variables were included in the model simultaneously, only systolic/diastolic ambulatory BP was a significant predictor of cardiovascular events (*P*=0.002/<0.001). Home systolic/diastolic BP improved the fit of the model only marginally when added to a model including office BP (χ^2=3.0/4.0, *P*=0.09/0.047). Ambulatory BP, however, improved the fit of model more clearly when added to office and home BP (χ^2=9.0/12.3, *P*=0.001/<0.001). Our findings suggest that ambulatory BP is prognostically superior to office and home BP. (*Hypertension*. 2014;64:281-286.) • **Online Data Supplement**

Key Words: blood pressure determination ■ blood pressure monitoring, ambulatory ■ diagnostic techniques, cardiovascular ■ hypertension

Home and ambulatory blood pressure monitoring offers specific advantages over office blood pressure measurements, such as a large number of measurements free from the white-coat effect. These benefits of out-of-office blood pressure monitoring have been also shown to translate into improved prognostic accuracy compared with office measurements.[1–5] Recently updated hypertension guidelines have, therefore, taken a step away from classic office blood pressure measurements being the gold standard for screening, diagnosing, and management of hypertension.[6,7] The 2011 British National Institute for Health and Care Excellence guidelines recommend primarily ambulatory blood pressure monitoring to confirm the diagnosis of hypertension, or if a person is unable to tolerate ambulatory monitoring, home monitoring should be used as a suitable alternative.[6] The 2 guidelines from the American, International, and European Societies of Hypertension published in 2013 take a slightly more conservative approach and propose that out-of-office blood pressure, either home or ambulatory, should be considered to confirm the diagnosis of hypertension.[7,8]

Twenty-four–hour ambulatory monitoring is a useful tool in diagnosing white-coat phenomena, masked hypertension, and nocturnal hypertension.[9] However, high cost and restricted availability of ambulatory monitoring systems often limit its use in general practice. In addition, ambulatory monitoring causes some discomfort and sleep disturbance in a large share of patients.[10] Home blood pressure monitoring offers most of the benefits of ambulatory monitoring without the previously mentioned disadvantages and it can be easily used for follow-up of treatment with repeated measurements. On the other hand, home blood pressure monitoring does not provide nighttime readings, and the readings are often subject to selection bias.[11]

Many cross-sectional and follow-up studies have shown that home and ambulatory blood pressure measurements are more strongly associated with hypertensive target organ damage and cardiovascular prognosis than is office blood pressure.[1–5,12–15] However, data comparing home versus ambulatory blood pressure in a prognostic setting are extremely scarce because only 2 studies with contradictory results and inadequate end points have been published.[16,17]

The clinical guidelines are moving from office measurements to out-of-office monitoring. Apart from the National Institute for Health and Care Excellence guidelines, ambulatory and home blood pressure measurements are considered complimentary rather than alternative methods. However, it is still unresolved whether ambulatory blood pressure is superior to home blood pressure in predicting overall cardiovascular outcome and should one method be possibly promoted as the primary method for diagnosing hypertension instead of the other. The main purpose of this study is to elucidate the prognostic significance of office versus home versus ambulatory blood pressure.

Methods

Study Population

The study population consisted of 2 cohorts, which were examined at the Rehabilitation Research Center of the Social Insurance Institution in Turku, Finland. The baseline assessments were similar for both cohorts. The study sample for the first cohort consisted of 340 men and women aged 34 to 64 years living in southwestern Finland who were randomly drawn from the population register. Two hundred seventy-five individuals (80.9%) agreed to participate in the study and were examined between February 1995 and February 1996. After excluding individuals with missing office, home, or blood pressure values, the first study cohort consisted of 264 participants.

The study sample for the second cohort consisted of 252 newly diagnosed and untreated hypertensive men and women aged 35 to 54 years. These patients were referred to the study by general practitioners and internists working in southwestern Finland and examined between September 1992 and October 1993. The patients were referred to the study if they had a mean systolic/diastolic blood pressure of 180 to 220/100 to 120 mm Hg in 2 blood pressure measurements performed in the primary healthcare system. After excluding individuals with missing office, home, or ambulatory blood pressure values, the second study cohort consisted of 238 participants. The 2 cohorts were analyzed both separately and together (n=502).

The study was conducted in compliance with the Second Declaration of Helsinki and was approved by the ethical committee of the Social Insurance Institution of Finland. All the participants gave their informed consent.

Blood Pressure Measurements

Office blood pressure was measured in the sitting position by a nurse between 8:00 and 10:00 AM with a mercury sphygmomanometer using first and fifth Korotkoff sounds.[18] Blood pressure was measured after the patient had rested for 15 minutes. The last 5 minutes of rest were spent with the cuff around the right upper arm. Blood pressure was recorded twice, with approximately a 2-minute interval. Office blood pressure was determined as the mean of the 4 duplicate blood pressure measures performed at 1-week intervals within 3 weeks.

Home blood pressure was self-measured with a validated automatic oscillometric device (Omron HEM 705C).[19] Patients received written instructions and individual guidance on how to measure blood pressure correctly. Preparations for self-measured home blood pressure were the same as for clinic blood pressure. Seated blood pressure was measured twice at a 2-minute interval every morning between 6:00 and 9:00 AM and every evening between 6:00 and 9:00 PM on 7 consecutive days. Home blood pressure was determined as the mean of 14 duplicate measures.

Ambulatory blood pressure was recorded with an auscultatory device (Suntech Accutracker II) that was validated according to the Association for the Advancement of Medical Instrumentation and British Hypertension Society protocols.[20] It fulfilled the criteria of the Association for the Advancement of Medical Instrumentation protocol for both systolic and diastolic blood pressures but only fulfilled the criteria for systolic blood pressure of the British Hypertension Society protocol.[20] Ambulatory blood pressure was recorded during daytime (6:00 AM to 11:00 PM) at 15-minute intervals and during nighttime (11:00 PM to 6:00 AM) at 30-minute intervals. Twenty-four–hour, daytime, and nighttime blood pressures were calculated from hourly means.

Follow-Up

Follow-up data were accumulated until December 31, 2011. The 10th version of the International Classification of Diseases, Injuries, and Causes of Death (ICD) is in use in Finnish death certificates and hospital discharge reports.

Mortality data were obtained from the national mortality register based on death certificates. Cardiovascular death was defined as mortality related to disease of the circulatory system (ICD-10 code "I"). Data on hospitalization attributable to heart failure and nonfatal coronary and stroke events were obtained from the national hospital discharge register. ICD codes I21 and I22 were classified as acute coronary events, ICD codes I60 to I64 as acute stroke events, and participants with ICD codes I11.0, I13.0, I13.2, and I50 were classified as being hospitalized because of acute heart failure. In addition, information on coronary interventions and coronary artery bypass graft surgery performed was obtained from the hospital discharge register. Cardiovascular diagnoses in these registers have been described and validated in detail previously and the registers cover every hospital in Finland.[21–23]

The primary end point was the combination of cardiovascular mortality, nonfatal myocardial infarction, nonfatal stroke, hospitalization for heart failure, percutaneous coronary intervention, and coronary artery bypass graft surgery. Only the first event was included in this analysis.

Statistical Analyses

Categorical variables were compared using the χ^2 test and continuous variables using the Student t test. We used Cox proportional hazard models for multivariate analyses. Association of office, home, and ambulatory blood pressures with the end points was analyzed by estimation of the hazard ratios and their 95% confidence intervals per 1/1 mm Hg increase in systolic/diastolic blood pressure. The models were adjusted for sex, age, use of antihypertensive medication, smoking status (daily use of tobacco products), body mass index, serum fasting glucose, and serum fasting total cholesterol. The likelihood ratio χ^2 value was used as a measure of the improvement of goodness of fit between the models that added home and ambulatory blood pressures to the data relating the risk of cardiovascular events to office blood pressure.

A probability value <0.05 was considered statistically significant. Data are reported as mean±SD. Database management and statistical analysis were performed with SAS software (SAS Institute, Cary, NC), version 9.2.

Results

The characteristics of the study population are reported in Table 1. Participants who had a cardiovascular event during follow-up were older and had a higher body mass index and fasting serum glucose than participants with no events ($P≤0.01$ for all). In addition, there were more men, smokers, and participants with antihypertensive medication among those who suffered a cardiovascular event ($P≤0.01$ for all). Participants who had a cardiovascular event had higher systolic and diastolic office, home, and ambulatory blood pressures ($P≤0.01$ for all).

The follow-up period ended on December 31, 2011, and the mean follow-up time was 16.1±3.9 years (median, 16.7 years), resulting in 8068 person-years of follow-up. A total of 70 subjects had ≥1 cardiovascular event (incidence, 8.7/1000 person-years) during the follow-up period. The first cardiovascular events were as follows: 19 nonfatal strokes, 16 nonfatal

Table 1.   Characteristics of Participants With and Without Cardiovascular Events During Follow-Up

Characteristic	Cardiovascular Events		P Value
	No (n=432)	Yes (n=70)	
Men, %	50	74	<0.001
Age, y	47±7	51±7	<0.001
BMI, kg/m^2	27±5	29±5	0.01
Total cholesterol, mmol/l	5.7±1.0	5.8±1.1	0.44
Glucose, mmol/l	5.3±0.7	5.8±1.5	<0.001
Blood pressure, mm Hg			
Office			
Systolic	131±17	142±18	<0.001
Diastolic	84±12	89±12	0.01
Ambulatory			
24-h			
Systolic	130±16	143±19	<0.001
Diastolic	79±10	85±10	<0.001
Daytime			
Systolic	136±16	149±20	<0.001
Diastolic	84±10	89±10	<0.001
Nighttime			
Systolic	115±17	128±20	<0.001
Diastolic	68±10	74±11	<0.001
Home			
Systolic	128±16	140±17	<0.001
Diastolic	84±12	90±12	<0.001
Smoking, %	19	31	0.01
Antihypertensive medication, %	5	17	<0.001
Cardiovascular disease, %	2	9	0.006

Values are shown as mean±SD or percentage. BMI indicates body mass index.

Table 2.   Hazard Ratios for Cardiovascular End Points in Relation to Office, Home, and Ambulatory Blood Pressures

BP Variable	Unadjusted Model		Adjusted Model	
	HR (95% CI)	P Value	HR (95% CI)	P Value
Systolic				
Office	1.027 (1.013–1.041)	<0.001	1.024 (1.009–1.040)	0.002
Home	1.036 (1.022–1.051)	<0.001	1.029 (1.013–1.045)	<0.001
24-h	1.034 (1.022–1.047)	<0.001	1.033 (1.019–1.047)	<0.001
Day	1.034 (1.021–1.047)	<0.001	1.032 (1.018–1.046)	<0.001
Night	1.029 (1.018–1.040)	<0.001	1.027 (1.015–1.040)	<0.001
Diastolic				
Office	1.016 (0.996–1.037)	0.11	1.018 (0.994–1.043)	0.14
Home	1.031 (1.010–1.053)	0.003	1.028 (1.005–1.052)	0.02
24-h	1.039 (1.015–1.063)	0.001	1.049 (1.023–1.077)	<0.001
Day	1.033 (1.010–1.057)	0.004	1.045 (1.019–1.071)	<0.001
Night	1.040 (1.019–1.061)	<0.001	1.043 (1.020–1.067)	<0.001

Hazard ratios (95% CIs) reflect the risk associated with a 1-mm Hg increase in systolic and diastolic blood pressures, respectively. In the adjusted model, hazard ratios were adjusted for age, sex, serum total cholesterol, serum total glucose, smoking, treatment with antihypertensive drugs, and body mass index. 95% CI indicates 95% confidence interval; BP, blood pressure; and HR, hazard ratio.

myocardial infarctions, 13 deaths of cardiovascular origin, 12 coronary interventions, and 10 hospitalizations for heart failure. There was no loss to follow-up because none of the participants had moved abroad.

In unadjusted Cox regression models, all blood pressures were predictive of cardiovascular events (Table 2). All blood pressure measurements were still predictive after adjustment for other risk factors for cardiovascular disease, except for diastolic office blood pressure (Table 2). The results were similar when the hazard ratios were calculated for a 1-SD, instead of a 1-mm Hg, increase in blood pressure (Table S1 in the online-only Data Supplement). Figure 1 shows the calculated absolute 16.1-year risk of cardiovascular events. The risk of cardiovascular events increased more steeply from office to home, day, 24-hour, and night blood pressures, although the differences were not as marked for systolic blood pressure as they were for diastolic blood pressure.

When systolic office, home, and 24-hour ambulatory blood pressures were entered in the same adjusted multivariate model (Table 3), only systolic ambulatory blood pressure was a significant predictor of cardiovascular events (P=0.002),

whereas systolic office (P=0.60) and home blood pressures (P=0.64) were not. Similar results were found when diastolic office, home, and ambulatory blood pressures were entered in the same model as only diastolic ambulatory blood pressure was a significant predictor of cardiovascular events (P<0.001), whereas diastolic office (P=0.08) and home blood pressures (P=0.70) were not. When the population cohort and the hypertensive cohort were analyzed separately, the results were similar in both cohorts (Table S2).

Table 4 shows the risk of cardiovascular events calculated by adding home and ambulatory systolic blood pressure values to the model obtained with office systolic blood pressure. Home systolic/diastolic blood pressure improved the goodness of fit of the model only marginally when added to a model including office blood pressure (χ^2=3.0/4.0, P=0.09/0.047). In contrast, 24-hour, day, and night blood pressure values improved the predictive ability of the model more clearly when added to office and home blood pressure values combined. In unadjusted models, home blood pressure improved the model fit more clearly when added to a model including office blood pressure (χ^2=9.8/10.1, P=0.002/0.001), whereas 24-hour blood pressure improved the fit of the model only marginally when added to office and home blood pressure values combined (χ^2=5.3/4.3, P=0.02/0.04).

Discussion

This study demonstrates that office, home, and ambulatory blood pressures are all predictive of cardiovascular events. However, ambulatory blood pressure values seem to provide prognostic information about cardiovascular risk above and beyond those of office and home blood pressures. The risk of cardiovascular events increases more steeply from office to home and ambulatory blood pressures.

Only 1 study has compared the prognostic accuracy of home versus ambulatory blood pressure on cardiovascular
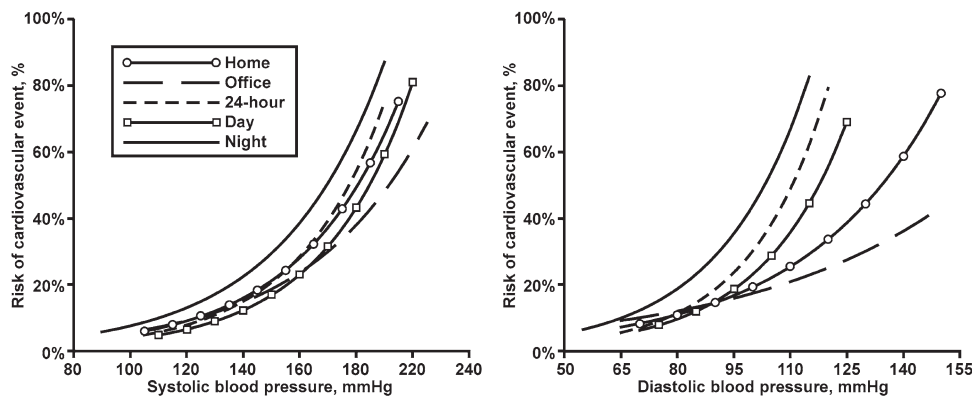
Figure. Office, home, and ambulatory blood pressures as predictors of 16.1-year risk of cardiovascular events. The values have been plotted to span the 5th to 95th percentile interval. The figure is adjusted for other cardiovascular risk factors.

end points previously. This report was based on the Italian Pressioni Arteriose Monitorate e Loro Associazioni cohort, which included a population sample of 2051 participants living in Monza, Italy.[16] The authors concluded the overall ability to predict death was not greater for home and ambulatory than for office blood pressure. However, the study had several limitations.[24–26] The analyses of the Pressioni Arteriose Monitorate e Loro Associazioni study were not adjusted for any potential confounders or other cardiovascular risk factors although age and body mass index have been shown to affect the within-subject differences between office and ambulatory blood pressures.[27] Furthermore, home blood pressure was based on the mean of only 2 home measurements, and cardiovascular mortality was the sole available end point. This explains why only 56 cardiovascular events were recorded during the relatively long 10.9 years of follow-up.

The Japanese Ohasama group also published a follow-up study of 1007 community-dwelling participants, which compared the prognostic value of office versus home versus ambulatory blood pressure.[17] The results of this study were somewhat ambiguous as home blood pressure was more closely associated with the risk of carotid atherosclerosis, whereas ambulatory blood pressure was more closely associated with silent cerebrovascular lesions. Furthermore, the study was limited by using only surrogate end points, silent cerebrovascular lesions, and carotid atherosclerosis to investigate the association between various methods of blood pressure measurement methods and cardiovascular risk.

In our study, which included both cardiovascular mortality and morbidity as end points and adjustment for other cardiovascular risk factors, the prognostic value of blood pressure measurements seemed to increase from office to home to ambulatory blood pressure. To us, as strong proponents of home blood pressure monitoring, this finding was somewhat surprising as in the cross-sectional phase of this study home blood pressure was slightly more strongly associated with left ventricular mass, and equally strongly associated with micro-albuminuria, than office or ambulatory blood pressure.[12] The causes underlying this finding are somewhat unclear because both home and ambulatory blood pressure monitoring provide a large number of out-of-office blood pressure measurements. Furthermore, both techniques can be used to detect white-coat and masked hypertension and thereby avoid over- and under-estimation of cardiovascular risk.[28,29] In our study, however, we tried to minimize the white-coat phenomenon by measuring office blood pressure meticulously (4 duplicate measurements at 1-week intervals). Our results could be explained by the fact

Table 3.   Hazard Ratios for Cardiovascular End Points in Relation to Office, Home, and Ambulatory Blood Pressures When All Blood Pressures Are Entered Simultaneously in the Model

BP Variable	HR (95% CI)	P Value
Systolic		
Office	0.992 (0.964–1.021)	0.60
Home	0.991 (0.956–1.028)	0.64
24-h	1.045 (1.017–1.074)	0.002
Diastolic		
Office	0.961 (0.919–1.004)	0.08
Home	0.990 (0.943–1.040)	0.70
24-h	1.096 (1.041–1.153)	<0.001

Hazard ratios (95% CIs) reflect the risk associated with a 1-mm Hg increase in systolic and diastolic blood pressures, respectively. Hazard ratios were adjusted for age, sex, serum total cholesterol, serum total glucose, smoking, treatment with antihypertensive drugs, and body mass index. 95% CI indicates 95% confidence interval; BP, blood pressure; and HR, hazard ratio.

Table 4.   Increases in Goodness of Fit by Progressively Adding Blood Pressure Variables

Model	Systolic		Diastolic	
	LR χ^2	P Value	LR χ^2	P Value
1. Office	74.4	…	67.3	…
2. Office+home*	3.0	0.09	4.0	0.047
3. Office+24-h*	11.8	0.001	16.1	<0.001
4. Office+day*	10.7	0.001	13.0	<0.001
5. Office+night*	8.6	0.003	11.8	0.001
6. Office+home+24-h†	9.0	0.003	12.3	<0.001
7. Office+home+day†	7.9	0.005	9.0	0.003
8. Office+home+night††	5.8	0.02	8.2	0.004

χ^2 value of 3.8 corresponds with P value of 0.05, 6.6 to 0.01, and 10.8 to 0.001. Data are adjusted for age, sex, serum total cholesterol, serum total glucose, smoking, treatment with antihypertensive drugs, and body mass index. LR indicates likelihood ratio.

*Increases in likelihood ratio χ^2 vs model 1.

†Increases in likelihood ratio χ^2 vs model 2.

that ambulatory measurements performed during normal daily activities provide a better estimate of the true prevailing blood pressure load than home measurements, which are always performed at rest. Despite the possible advantages of ambulatory blood pressure monitoring in diagnosing hypertension, repeated ambulatory monitoring during follow-up of treatment every 3 to 6 months is not usually feasible because of poor availability in primary care, lack of resources, and the discomfort caused by ambulatory monitoring in many patients.[10]

The risk of cardiovascular events increased more steeply from office to home and ambulatory blood pressures, which is in line with the findings of several previous studies.[1–5] This finding by itself does not necessarily imply a greater predictive ability but does highlight the importance of having separate diagnostic thresholds for office, home, and ambulatory blood pressures. Especially, primary care physicians should be educated on the importance of using separate outcome-driven thresholds for out-of-office blood pressure for rational treatment decisions.[30,31]

Although our study had a fairly long follow-up time of 16.1 years, the relatively small size of our cohort and the limited number of events did not enable us to perform subgroup analyses and restricts the generalizability of our results. Although the benefits of home and ambulatory blood pressures have been demonstrated in several previous studies, our results need to be validated in other, larger populations before any definite conclusions on the prognostic superiority of ambulatory over home blood pressure can be made.[1–5] Furthermore, the ambulatory monitor used in our study passed the validation standard of the Association for the Advancement of Medical Instrumentation protocol but not of the British Hypertension Society protocol in that it failed to satisfy the criteria for diastolic blood pressure. As a consequence, this study can only base its conclusions on systolic blood pressure with a caveat about diastolic blood pressure.

Perspectives

The prognostic value provided by various methods of blood pressure measurement seems to increase from office to home to ambulatory measurements. The findings of our study support the role of ambulatory monitoring as the gold standard of blood pressure measurement and the ongoing trend of moving from office measurements to out-of-office blood pressure monitoring when diagnosing and treating hypertension.

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Disclosures

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Novelty and Significance

What Is New?

- Home and ambulatory blood pressures have both been shown to be stronger predictors of cardiovascular risk than office blood pressure.
- Data comparing home versus ambulatory blood pressure in a prognostic setting are extremely scarce.

What Is Relevant?

- The prognostic value provided by various methods of blood pressure measurement seems to increase from office to home to ambulatory measurements.

Summary

The findings of our study support the role of ambulatory monitoring as the gold standard of blood pressure measurement and the ongoing trend of moving from office measurements to out-of-office blood pressure monitoring when diagnosing and treating hypertension.