

Ambulatory Blood Pressure Monitoring and Risk of Cardiovascular Disease: A Population Based Study

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Background: Information on the relationship between ambulatory blood pressure (BP) and cardiovascular disease in the general population is sparse.

Methods: Prospective study of a random sample of 1700 Danish men and women, aged 41 to 72 years, without major cardiovascular diseases. At baseline, ambulatory BP, office BP, and other risk factors were recorded. The end point was a combined end point consisting of cardiovascular mortality, ischemic heart disease, and stroke.

Results: After a mean follow-up of 9.5 years, 156 end points were recorded. In multivariate models, the relative risk (95% confidence interval) associated with increments of 10/5 mmHg of systolic/diastolic ambulatory BP were 1.35 (1.21–1.50) and 1.27 (1.16–1.39). The corresponding figures for office BP were 1.18 (1.09–1.29) and 1.11 (1.03–1.19). Compared with normotension (office BP <140/90 mm Hg; daytime BP <135/85 mm Hg) the relative risks associated with isolated office hypertension (office BP ≥140/90 mm Hg; daytime BP <135/85 mm Hg), isolated ambulatory hypertension (office BP <140/90

mm Hg; daytime BP ≥135/85 mm Hg), and sustained hypertension (office BP ≥140/90 mm Hg; daytime BP ≥135/85 mm Hg) were 0.66 (0.30–1.44), 1.52 (0.91–2.54), and 2.10 (1.45–3.06), respectively. A blunted BP decrease at night was a risk factor ($P = .02$) in subjects with daytime ambulatory hypertension, but not in subjects with daytime ambulatory normotension ($P = .13$).

Conclusions: Ambulatory BP provided prognostic information about cardiovascular disease better than office BP. Isolated office hypertension was not a risk factor and isolated ambulatory hypertension tended to be associated with increased risk. A blunted BP decrease at night was a risk factor in subjects with daytime ambulatory hypertension. *Am J Hypertens* 2006;19: 243–250 © 2006 American Journal of Hypertension, Ltd.

Key Words: Ambulatory blood pressure, blood pressure measurement, hypertension, cardiovascular disease, prognosis, epidemiology.

In patients with hypertension multiple measurements of blood pressure (BP) during a 24-h period (ambulatory BP) is superior to a few measurements in a doctor's office (office BP) for estimating the risk of future cardiovascular morbidity and mortality.^{1–4} Evidence is accumulating that ambulatory BP is also superior to office BP for estimating the risk of mortality in the general population.^{5–7} As for morbidity in the general population, only a single study has examined the value of ambulatory BP for the prediction of stroke in a Japanese population.⁸

Ambulatory BP and office BP are only moderately correlated and based on selected cutoff values. Many sub-

jects appear to have isolated office hypertension, often called white coat hypertension (that is hypertension in the office but normal ambulatory BP), or isolated ambulatory hypertension, often called masked hypertension (that is normal BP in the office but hypertension on ambulatory BP monitoring).^{9,10}

In 1993 to 1994, we recorded ambulatory BP in a random sample of 1700 men and women from the general Danish population. After 10 years of follow-up, we have shown that ambulatory BP was a better predictor of all-cause and cardiovascular mortality than office BP in this population.⁶ In the present article, we expanded our results

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to a combined end point also dealing with morbidity. In addition, we studied BP as a categorical variable and wanted to address the prognostic value of isolated office hypertension, isolated ambulatory hypertension, and dipping versus nondipping.

Methods

Study Population

In 1982 to 1984, a random sample of 4581 Danes participated in the MONItoring of trends and determinants in Cardiovascular Disease (MONICA 1) health survey.¹¹ Participants were selected to represent an equal number of men and women aged 30, 40, 50, and 60 years. Eventually, 3785 (83%) participated. In 1993 to 1994, the participants were invited to be examined again.¹² Of these 2656 (70%) were willing to participate and gave written informed consent. The study was performed in the Research Center for Prevention and Health in Glostrup. All subjects completed a questionnaire on current and prior diseases, intake of medication, and cardiovascular risk factors. The study was conducted in accord with the Second Helsinki Declaration and approved by the ethics committee for Copenhagen Country.

Criteria of Exclusion

For the present study, 956 subjects were initially excluded (574 because of technical problems or unwillingness to participate in the ambulatory BP monitoring, 240 with too few ambulatory BP readings according to recommendations,¹³ 13 worked at night, and 129 with a prior diagnosis of myocardial infarction or stroke, or taking digoxin or nitrates) leaving 1700 (64%) men and women eligible.

Data Collection

Office BP was measured at rest with a random zero mercury sphygmomanometer and the mean of two measurements was reported. Oscillometric ambulatory BP measurements were recorded using a Takeda TM-2421 (A&D, Tokyo, Japan) device, which has passed validation tests.¹⁴ The BP recordings were made every 15 min between 7 AM and 11 PM, and every 30 min between 11 PM and 7 AM. Means of ambulatory BP were computed with weights according to the time interval between successive readings. The discrimination between daytime and night-time was based on a diary, and when this information was inadequate ($n = 111$) we defined daytime as the interval between 6 AM and midnight and night-time from midnight to 6 AM.

Fasting concentrations of insulin, glucose, and lipids were analyzed by standard methods, and other baseline risk factors were obtained as described in detail elsewhere.¹⁵

Classification of Subjects

According to the latest consensus,^{13,16,17} we defined the following categories of hypertension: isolated office hy-

pertension (office BP ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic together with daytime BP < 135 mm Hg systolic and < 85 mm Hg diastolic), isolated ambulatory hypertension (office BP < 140 mm Hg systolic and < 90 mm Hg diastolic together with daytime BP ≥ 135 mm Hg systolic or ≥ 85 mm Hg diastolic office BP), and sustained hypertension (office BP ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic together with daytime BP ≥ 135 mm Hg systolic or ≥ 85 mm Hg diastolic office BP). Normotension was defined as office BP < 140 mm Hg systolic and < 90 mm Hg diastolic together with daytime BP < 135 mm Hg systolic and < 85 mm Hg diastolic office BP. In addition, we defined nondipping as a decrease in systolic and diastolic BP of less than 10% from day to night,¹⁸ and calculated systolic and diastolic night-to-day ratio as the ratio between night-time and daytime BP.

End Points

Complete follow-up regarding death was obtained through information from the Civil Registration System. Information on cardiovascular mortality was obtained from blinded classification of death certificates and information on hospitalizations was recorded from The Danish National Health Register, which is known to have high sensitivity and predictive value.¹⁹

The predefined end point in this study was the combination of cardiovascular mortality, ischemic heart disease (ICD-8 code 410 to 414 or ICD-10 codes I20 to I25), and stroke (ICD-8 codes 431, 433, or 434 or ICD-10 codes I61 or I63).

Statistical Analysis

All analyses were performed with the Statistical Analysis System (SAS), version 8.2. Baseline characteristics were compared with Kruskal-Wallis test for continuous variables and χ^2 tests for categorical variables. The independent effect of several prognostic factors was tested by multivariate Cox proportional-hazard models. For the participants who experienced multiple events, the analysis included only the first event. With respect to potential covariates or confounders we only included variables that were significantly related to our outcome variable as determined in Cox proportional-hazard models with forward and backward selection. We tested all the variables listed in Table 1 and the P value for independent covariates to enter or stay in the model was set at .05. Both approaches gave the same results. The significance of adding few or many BPs to the ambulatory BP value was assessed by examining the change in $-2\log$ likelihood as consecutive 2-h periods were added to the model. The scale was set to show increments of 3.841 equivalent to a significant increase ($P = .05$) by the likelihood ratio test. The assumption of linearity and the proportional hazard assumption were tested. Interaction was tested with a likelihood ratio

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