

Prognostic Value of Systolic and Diastolic Blood Pressure in Treated Hypertensive Men

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Background: The aim of this study was to assess the cardiovascular risk in hypertensive subjects according to systolic blood pressure (SBP) and diastolic blood pressure (DBP) levels.

Methods: The study sample consisted of 4714 hypertensive men, treated by their physician, who had a standard health checkup at the d'Investigations Préventives et Cliniques Center, Paris, France, between 1972 and 1988. Cardiovascular disease (CVD) and coronary heart disease (CHD) mortality were assessed for a mean period of 14 years.

Results: Among treated subjects, 85.5% presented uncontrolled values for SBP (≥ 140 mm Hg) and/or DBP (≥ 90 mm Hg). After adjustment for age and associated risk factors, these subjects presented an increased risk for CVD mortality (risk ratio [RR], 1.66; 95% confidence interval [CI], 1.04-2.64) and for CHD mortality (RR, 2.35; 95% CI, 1.03-5.35) compared with controlled subjects. After adjustment for age, associated risk factors, and DBP, and

compared with subjects with SBP under 140 mm Hg, the RR for CVD mortality was 1.81 (95% CI, 1.04-3.13) in subjects with SBP between 140 and 160 mm Hg and 1.94 (95% CI, 1.10-3.43) in subjects with SBP over 160 mm Hg. By contrast, after adjustment for SBP levels, CVD risk was not associated with DBP. Compared with subjects with DBP under 90 mm Hg, RR for CVD mortality was 1.17 (95% CI, 0.80-1.70) in subjects with DBP between 90 and 99 mm Hg and 1.03 (95% CI, 0.67-1.56) in subjects with DBP over 100 mm Hg. Similar results were observed for CHD mortality.

Conclusions: In hypertensive men treated in clinical practice, SBP is a good predictor of CVD and CHD risk. Diastolic blood pressure, which remains the main criterion used by most physicians to determine drug efficacy, appears to be of little value in determining cardiovascular risk. Evaluation of risk in treated individuals should take SBP rather than DBP values into account.

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THE SIXTH Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure¹ and the recent report of the World Health Organization/International Society of Hypertension² classified blood pressure (BP) into stages based on either systolic (SBP) or diastolic (DBP) levels. Both classifications define the lowest SBP and DBP levels as being optimal, and the highest levels of both as having the highest cardiovascular morbidity and mortality rates. In the past few years, the importance of SBP has been emphasized, especially in older subjects,^{3,4} and more recently, it has been proposed that DBP values could be the best predictor of cardiovascular risk in younger subjects⁵ and SBP or pulse pressure in older subjects.

It has been suggested that SBP should be under 140 mm Hg and that DBP be under 90 mm Hg for all treated hypertensive

subjects, unless diabetes or target organ damage are present, in which case lower BP levels ($< 130/85$ mm Hg) should be targeted.^{1,2} Observational studies from several countries have demonstrated that

*For editorial comment
see page 506*

among treated hypertensive individuals, the proportion of those who are well controlled is less than 30%,^{6,7} and a recent survey in the United Kingdom indicated that only 6% of hypertensive subjects presented BP levels below the limit of 140/90 mm Hg.⁸

One of the reasons for these results may be the relative complexity of the guidelines that include SBP and/or DBP in the various classifications. In addition, physicians may not be convinced that the results found among hypertensive subjects participating in controlled studies,

METHODS

THE IPC POPULATION

The subjects were examined at the IPC Center. The IPC Center is subsidized by the French National Health Care system (Sécurité Sociale-Caisse Nationale d'Assurance Maladie) and provides all working and retired persons and their families with a free medical examination every 5 years. It is one of the largest medical centers of this kind in France, having carried out approximately 20 000 to 25 000 examinations per year since 1970 for people living in the Paris area.^{9,10}

Supine BP was measured 3 times in the right arm after a 10-minute rest period, using a manual sphygmomanometer. The mean of the last 2 measurements was calculated. The first and the fifth Korotkoff phases were used to define SBP and DBP. Tobacco use (current consumption of more than 10 cigarettes per day), and personal history of diabetes and hypertension were assessed with a self-administered questionnaire. Total cholesterol was measured at the IPC Center under fasting conditions, the day of the examination.

The IPC Center received approval from the national ethics committee (Comité National d'Informatique et des Libertés) to conduct these analyses. All subjects included in this analysis gave their informed consent at the time of the examination. Among these subjects, 75% were white-collar workers. Based on the national statistics on mortality, our cohort presented a 30% lower mortality rate than the general French population. This may be explained by the fact that people who come for a medical examination are generally healthy and motivated. Interestingly, when compared with the national data, the distribution of the different causes of mortality in our cohort was identical to that of the general population.

In the present analysis, all treated hypertensive men ($n=4714$) who had an examination at the IPC Center between 1972 and 1988 were included. Upon study entry, among the 4714 subjects, 112 (2.4%) had concurrent

cardiovascular disease (CVD), and the percentage of CVD did not vary according to SPB or DBP groups.

For all subjects, mortality data were obtained for a 9- to 25-year period (mean \pm SD, 14.0 \pm 4.2 years) that extended from the time of inclusion through December 1997. These data were obtained from the mortality records at the Institut National de Statistiques et d'Etudes Economiques, following a previously established procedure.^{9,10} Causes of mortality, taken from the death certificates, were provided by INSERM's (Institut National de la Santé et de la Recherche Médicale) Department of Mortality Studies (Unit SC 8). Causes of death were codified according to the eighth revision of the *International Classification of Diseases* until 1978 and the ninth revision thereafter. Cardiovascular-related deaths were coded 390-459, and 798 for sudden death. Coronary-related deaths were coded 410-414, and 798 for sudden death.

DATA ANALYSIS

In the present analysis, we used the current cut points proposed by the International Society of Hypertension and the World Health Organization. Subjects were considered as controlled by treatment when SBP was under 140 mm Hg and DBP was under 90 mm Hg (**Table 1**). Subjects were also divided into groups according to SBP (<140, 140-159, \geq 160 mm Hg) or DBP (<90, 90-99, \geq 100 mm Hg) to assess the specific roles of SBP and DBP, respectively (**Table 2** and **Table 3**). Differences in clinical characteristics and mortality rates according to BP levels were studied using either the *t* test or the χ^2 test. Analyses were carried out to evaluate risk ratios (RRs) and 95% confidence intervals (CIs) for CVD mortality using a Cox proportional hazard regression analysis. Multivariate models including age, total cholesterol, smoking, and diabetes were used to evaluate adjusted RR. The associations between SBP and CVD or CHD mortality were also considered after adjustment for DBP, and the associations between DBP and CVD or CHD mortality were also considered after adjustments for SBP.

All statistical analyses were carried out using the SAS statistical software package (SAS Institute Inc, Cary, NC).

which show the benefits of low BP levels (<140/90 mm Hg), are applicable to hypertensive subjects treated in their everyday clinical practices.

In this observational study, the prognostic value of SBP and DBP levels on cardiovascular mortality, especially coronary heart disease (CHD) mortality in hypertensive subjects, treated in "everyday" clinical practice, was assessed. The study sample consisted of 4714 treated hypertensive men from the Centre d'Investigations Préventives et Cliniques (IPC) cohort.

RESULTS

In the study population, age (mean \pm SD) was 52 \pm 11 years; SBP, 152 \pm 18 mm Hg; and DBP, 94 \pm 12 mm Hg. Only 14.5% of the patients presented controlled values for both SBP and DBP, 10.8% presented uncontrolled values for SBP alone, 4.2% presented uncontrolled values for DBP alone, and 70.5% of the treated hypertensive men presented uncontrolled values for both. Compared with sub-

jects with controlled BP values, those with high BP values had a statistically significant increase in multivariate-adjusted RR for CVD mortality (1.66; 95% CI, 1.04-2.64) and for CHD mortality (2.35; 95% CI, 1.03-5.35) (Table 1).

Table 2 shows CVD mortality rates and adjusted RRs according to the SBP and DBP categories. There was a 4-fold increase in unadjusted CVD mortality rates in subjects with SBP of 160 mm Hg or higher compared with subjects with SBP under 140 mm Hg. After adjustment for age, there was a 2.2-fold increase in CVD mortality (**Figure A**). As shown in the Figure, the relationship between SBP and CVD risk was linear. The group with SBP between 140 and 159 mm Hg showed a 63% ($P<.01$) increase in age-adjusted CVD mortality compared with the group with SBP under 140 mm Hg. After adjustment for age and associated risk factors, the risk for CVD mortality increased in the group with SBP between 140 and 160 mm Hg by almost 70% compared with the group with SBP under 140 mm Hg (Table 2). In the group with SBP

Table 1. Mortality Rates and Risk Ratios in Men With Controlled and Uncontrolled Hypertension*

	Controlled (n = 684)	Uncontrolled (n = 4030)	P Value
Age, mean (SD), y	48.3 (10.2)	52.7 (10.5)	<.001
SBP, mean (SD), mm Hg	129 (6)	156 (17)	<.001
DBP, mean (SD), mm Hg	79 (5)	97 (11)	<.001
Cholesterol, mean (SD) mg/dL†	226 (40)	234 (40)	<.001
Smokers, %	26.6	23.9	.17
Diabetes, %	14.5	15.5	.52
CVD mortality rate, % (No.)	2.63 (18)	6.77 (273)	<.001
CHD mortality rate, % (No.)	0.73 (5)	2.93 (118)	<.001
RR‡ (95% CI) for CVD mortality	1	1.66 (1.04-2.64)	<.05
RR‡ (95% CI) for CHD mortality	1	2.35 (1.03-5.35)	<.05

*SBP indicates systolic blood pressure; DBP, diastolic blood pressure; CVD, cardiovascular disease; CHD, coronary heart disease; RR, risk ratio; and CI, confidence interval.

†To convert cholesterol from milligrams per deciliter to millimoles per liter, multiply by 0.02586.

‡Risk ratios for men with uncontrolled vs controlled hypertension adjusted for age, total cholesterol, smoking, and diabetes.

of 160 mm Hg or higher, RR for CVD mortality was 2.5 times greater than in the reference group. After complementary adjustment for DBP levels, the risk of CVD mortality was still significantly higher in the group with SBP over 140 mm Hg compared with the group with SBP under 140 mm Hg.

When subjects were classified according to DBP levels, those with DBP over 100 mm Hg showed less than a 2-fold increase in CVD mortality compared with subjects with DBP under 90 mm Hg (Table 2). After adjustment for age, the relationship between DBP levels and CVD mortality was not significant (Figure, B). After adjustment for age and associated risk factors, the risk for CVD mortality in the group with DBP between 90 and 99 mm Hg did not increase significantly, whereas in the group with DBP over 100 mm Hg, it increased by 60% (Table 2). However, after adjustment for SBP, there was no association between DBP levels and CVD mortality.

The role of SBP and DBP on cardiovascular mortality was not influenced by age (interaction term age × SBP, $P = .44$ and age × DBP, $P = .80$).

Table 3 shows CHD mortality rates and adjusted RRs according to the SBP and DBP categories (Figure). Based on SBP and DBP levels, very similar results to those observed for CVD mortality were found. Once again, the roles of SBP and DBP in CHD mortality were not influenced by age (interaction term age × SBP, $P = .65$ and age × DBP, $P = .54$).

The association between pulse pressure and CVD mortality and CHD mortality was also evaluated. The results from these analyses showed that pulse pressure had the same predictive value as SBP (data not shown).

COMMENT

Our data show that more than 85% of the treated hypertensive men had uncontrolled SBP or DBP levels. Among

Table 2. Mortality Rates and Adjusted Risk Ratios for CVD Mortality According to SBP and DBP Groups in Men Treated for Hypertension*

Group	Unadjusted Mortality Rates†	RR Adjusted for Age and Associated Risk Factors‡ (95% CI)	RR Adjusted for Age, Associated Risk Factors,‡ and BP§ (95% CI)
SBP, mm Hg			
<140	15.4 (19)	1	1
140-159	37.4 (110)	1.69 (1.03-2.76)	1.81 (1.04-3.13)
≥160	66.6 (162)	2.52 (1.56-4.09)	1.94 (1.10-3.43)
DBP, mm Hg			
<90	31.7 (53)	1	1
90-99	42.1 (99)	1.31 (0.94-1.83)	1.17 (0.80-1.70)
≥100	53.9 (139)	1.60 (1.16-2.20)	1.03 (0.67-1.56)

*CVD indicates cardiovascular disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; RR, risk ratio; CI, confidence interval; and BP, blood pressure.

†Per 10 000 person-years (absolute number).

‡Associated risk factors are total cholesterol, tobacco consumption, and diabetes.

§DBP or SBP adjusted, whichever is appropriate.

Table 3. Mortality Rates and Adjusted Risk Ratios for CHD Mortality According to SBP and DBP Groups in Men Treated for Hypertension*

Group	Unadjusted Mortality Rates†	RR Adjusted for Age and Associated Risk Factors‡ (95% CI)	RR Adjusted for Age, Associated Risk Factors,‡ and BP§ (95% CI)
SBP, mm Hg			
<140	4.9 (6)	1	1
140-159	17.1 (50)	2.54 (1.08-5.96)	2.09 (0.93-5.28)
≥160	27.6 (67)	3.51 (1.51-8.20)	2.96 (1.12-7.84)
DBP, mm Hg			
<90	14.2 (21)	1	1
90-99	17.0 (40)	1.33 (0.78-2.27)	1.18 (0.65-2.13)
≥100	24.1 (62)	1.72 (1.05-2.84)	1.11 (0.58-2.12)

*CHD indicates coronary heart disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; RR, risk ratio; CI, confidence interval; and BP, blood pressure.

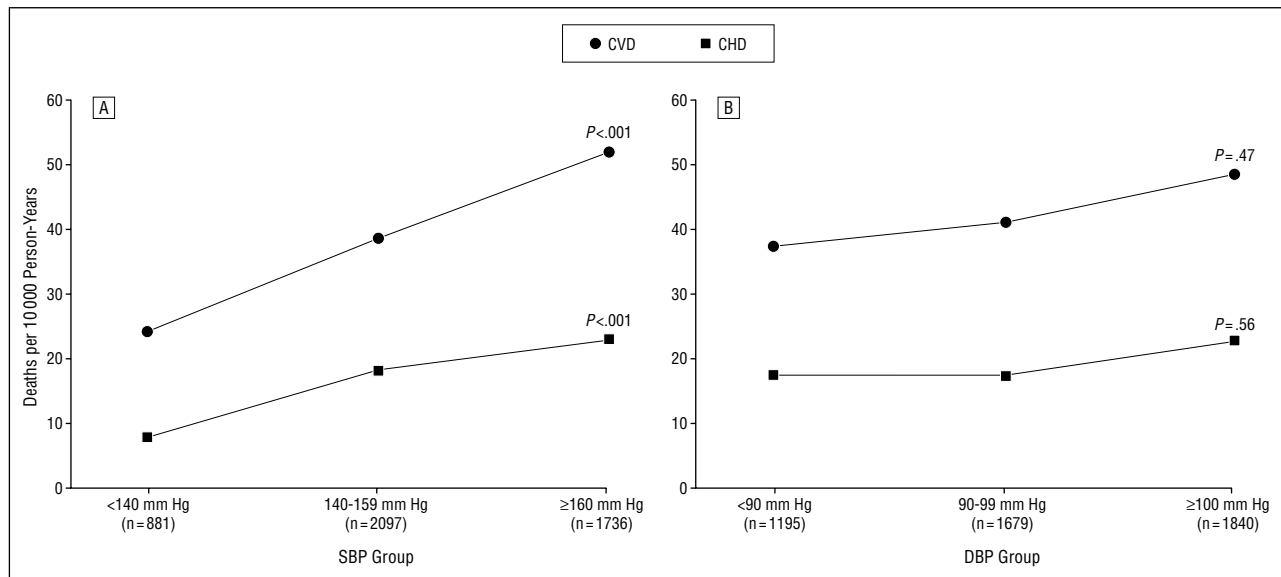
†Per 10 000 person-years (absolute number).

‡Associated risk factors are total cholesterol, tobacco consumption, and diabetes.

§DBP or SBP adjusted, whichever is appropriate.

them, most (70%) had high levels of both SBP and DBP, followed by those with high SBP and controlled DBP. This clearly confirms that, as measured in a clinical setting, a controlled BP, especially SBP, is uncommon. The most important result of this study is that cardiovascular mortality, especially CHD mortality, is much higher in uncontrolled hypertensive men than in controlled hypertensive men, and that SBP levels, but not DBP levels, can predict CVD risk independent of age.

It is well documented that reducing BP is associated with a decrease in the risk of coronary and cerebrovascular complications. A meta-analysis of 14 controlled clinical trials demonstrated that lowering DBP by



Age-adjusted cardiovascular disease (CVD) and coronary heart disease (CHD) mortality rates according to systolic blood pressure (SBP) (A) and diastolic blood pressure (DBP) (B) levels in men treated for hypertension.

6 mm Hg reduced cerebrovascular morbidity and mortality by 42% and the risk of CHD by 14%.¹¹ The Hypertension Optimal Treatment trial also confirmed that reduction in DBP with treatment decreased CVD risk by 30%.¹² Although the benefits of reducing DBP were clearly shown in numerous controlled studies in younger and older patients with systolic-diastolic hypertension, recent findings suggest that normalization of SBP rather than DBP should be the main goal of antihypertensive treatment.¹³⁻¹⁶ The benefits of treating high SBP, especially in older subjects, were established by the Systolic Hypertension in the Elderly Program¹³ and the Systolic Hypertension Europe¹⁴ trials in older subjects with isolated systolic hypertension, but also in patients with an increase in both SBP and DBP.^{15,16} Our results were obtained from subjects who were not a part of a specific research program and were followed up by their own physicians. This study can therefore better evaluate the long-term CVD risk in hypertensive subjects followed up and treated by their physicians according to the standard clinical practice. Under these conditions that reflect the regular treatment of French hypertensive persons, we confirmed the results of several studies showing that getting SBP to goal levels is much more difficult than controlling DBP levels.^{6-8,17} The new element provided by our study is that lack of SBP control may be a major determinant of the increased morbidity and mortality in treated hypertensive persons reported by other population studies.^{18,19} Also, under these circumstances, the level of DBP in treated men does not seem to be of a significant prognostic value.

As shown in Table 2 and the Figure, CVD mortality was 60% higher in men with DBP values over 100 mm Hg compared with those with DBP values under 90 mm Hg. However, this was mainly because most subjects with high DBP also had high SBP; thus, after adjustment for SBP, DBP levels lost all predictive value. On the other hand, the RR for adjusted CVD and CHD mortality was approximately 2.5 times higher in treated hypertensive men with SBP values over 160 mm Hg com-

pared with those with SBP values under 140 mm Hg. It is important to note that the predictive value of SBP remained significant even after adjustment for DBP levels. It is also interesting to point out that the presence of an SBP between 140 and 160 mm Hg (corresponding to a "mild" increase in SBP) under treatment is accompanied by a 2-fold increase in CVD and CHD age-adjusted mortality compared with treated subjects with well-controlled SBP levels. This result is important in terms of public health since a large proportion of treated hypertensive persons fall into this group (44.5% in our study).

The role of SBP and DBP in predicting CVD and CHD risk in our population was not influenced by age. However, it has previously been reported in a general population that DBP better reflects the CVD risk in younger subjects and that SBP better reflects the risk in older subjects.⁵ These differences may be explained by the fact that low DBP in treated subjects may not have the same significance as low DBP in untreated subjects. Diastolic BP levels are influenced by arterial or arteriolar alterations in opposite ways: an increase in peripheral vascular resistance leads to an elevation in DBP, whereas stiffening of large arteries can contribute to a decrease in DBP.^{20,21} Since stiffness is a major sign of arterial aging, it could also be suggested that subjects receiving treatment have a more advanced arterial age than chronological age. This could explain why what is found for older subjects in the general population is observed even in younger treated hypertensive subjects.

There were some study limitations. Although the age range of this population was very large (19-91 years), the large majority of subjects were middle-aged men (52±11 years), with fewer individuals at the extremes. Therefore, it is possible that the lack of interaction between age and the role of SBP or DBP may not be valid in younger (<40 years) or older (>65 years) subjects. Another limitation is that we included only men. In previous studies that included both normotensive and hypertensive sub-

jects of the IPC Center cohort, the predominant roles of SBP and pulse pressure were observed in men, but not in women.^{22,23} Due to the lower CVD mortality rates in women, especially CHD mortality rates, the lack of statistical power prevented us from carrying out the same analyses in women.

It is also important to note that single-visit BP measurements could overestimate the percentage of uncontrolled treated subjects. However, this study clearly shows that under these circumstances, similar to those faced by physicians in the follow-up of their treated hypertensive patients, an SBP value over 140 mm Hg is strongly associated with high CVD mortality in treated men.

The lack of predictive value of DBP may be because patients with high DBP levels were subsequently more likely to receive more aggressive treatment than those with high SBP. This was especially true in the 1980s when isolated systolic hypertension was not uniformly treated. Although this hypothesis could partially explain the observed lack of predictive value of DBP, all recent studies show that the high DBP values were not normalized in a majority of treated hypertensive subjects.⁶⁻⁸ Therefore, it cannot be assumed that subjects with high DBP levels were subsequently normalized and that this was the reason for the lack of association between DBP levels and CVD and CHD mortality.

In conclusion, in treated hypertensive men, SBP is a good predictor of CVD and CHD risk. Diastolic BP, which remains the main criterion used by most physicians in determining drug efficacy, appears to be of little value in determining CVD risk. Our results show that in clinical practice, a well-controlled SBP (<140 mm Hg) should be the goal of antihypertensive treatment.

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