Original Article

Association between Blood Pressure and Mortality in 80-Year-Old Subjects from a Population-Based Prospective Study in Japan

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Hypertension is one of the greatest risk factors for cardiovascular disease, but the contribution of high blood pressure to cardiovascular morbidity and mortality is weakened with aging. In the present study, we examined whether high blood pressure would be a risk factor for total and cardiovascular mortality in a group of very elderly Japanese. Six hundred and thirty-nine participants who were 80 years old in 1997 were enrolled. The subjects were divided into three groups on the basis of their systolic blood pressure (SBP) (below 140 mmHg [group 1, *n*=212], from 140 mmHg to 159 mmHg [group 2, *n*=217], over 160 mmHg [group 3, *n*=210]). During the 4-year follow-up period, 87 individuals died and 24 of these deaths were due to cardiovascular diseases. Cox multivariate regression analysis revealed that there was no association between total mortality and SBP levels (relative risk [RR] 1.71; confidence interval [CI] 0.81–3.58; group 3 compared with group 1, *p*=0.35). However, the subjects taking antihypertensive medication showed significantly higher mortality with increasing SBP level (RR 5.72, CI 1.03–31.6, *p*=0.04, group 3 compared with group 1). Furthermore, in the subjects with a cardiovascular disease such as angina or stroke, high SBP increased the total mortality (RR 13.4, CI 2.39–75.1, *p*=0.004, group 3 compared with group 1). The present study did not find an association between blood pressure and mortality in the very elderly. However, our results did suggest that high SBP increases the risk of mortality in patients with cardiovascular diseases and/or taking antihypertensive medication. (*Hypertens Res* 2008; 31: 265–270)

***Key Words*: systolic blood pressure, mortality, cross sectional study, elderly**

Introduction

It is clear that hypertension is an important risk factor of cardiovascular disease in the young and middle-aged populations. A large scale meta-analysis has shown the relevance of cardiovascular mortality and blood pressure (BP) at ages 40–89, but the contribution of high BP to cardiovascular mortality decreases with advancing age (*1*). There have been several reports investigating the relationship between BP and mortality of the very old (*2–13*). However, the results of these studies are not consistent; some studies found the highest mortality in the subjects with the lowest BP (*2–9*) while others showed a positive linear (*1*, *11*) or U-shaped association (*12*, *13*) between BP and mortality. Japan is rapidly becoming an aging society, and the very elderly—those age 80 years or over—now represent about 3.4% of the population (*14*) (http://wwwdbtk.mhlw.go.jp/toukei/index.html), but there

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has been only one study examining the correlation between BP and mortality in this age group in Japan (*13*). The 8020 Data Bank Survey, a unique cross-sectional survey conducted in Japan, was originally designed to explore the relationship between the systemic and dental health conditions of very elderly subjects. In the present study, we use the data from this survey to clarify whether BP correlates with total or cardiovascular mortality in the very elderly Japanese general population.

Methods

Study Population

This study was part of a community-based cross-sectional survey called the 8020 Data Bank Survey, which was conducted in Japan. The 8020 Data Bank Survey was designed to collect baseline data on the systemic and dental health conditions in 80-year-old subjects and to promote the idea that everyone should still have at least 20 original teeth by the age of 80. All participants were born in 1917, and thus were 80 years old in 1997 when the initial screening was conducted. The data were gathered from 9 districts (Buzen City, Munakata City, Yukuhashi City, the Tobata Ward of Kitakyushu City, Kanda Town, Katsuyama Town, Toyotsu Town, Tsuiki Town and Shinyoshitomi Village) in Fukuoka Prefecture, Japan. The total number of people born in 1917 in these 9 districts was 1244. Six hundred and ninety-seven of these residents (278 men and 419 women) participated, and 639 (256 men and 383 women) participants completed the physical and blood examination and were enrolled in the following analysis. Because the gender distributions differed significantly among these 9 districts, the data for each participant was adjusted for the district in which he or she lived. For each individual who died during this period, we recorded the date and cause of death according to resident registration cards and official death certificates. The cause of death was classified according to the 10th version of the International Classification of Disease (ICD-10), and there was no loss to follow-up during the 4 years. All participants were ambulatory in their daily life. This study was approved by the Human Ethics Committee of Kyushu Dental College. The details of the study protocol were explained to the subjects, and informed consent was obtained prior to participation.

Data Collection

The examination included completion of a medical questionnaire, which contained questions regarding smoking history, physical activity, and alcohol consumption. The activities of daily living (ADL) status was determined by public health nurses who classified subjects into six groups. Individuals in ADL-1 (n=541) were mostly independent in everyday life; they left home on their own and used transportation to go wherever they wanted. Those in ADL-2 (n=71) were also nearly independent in everyday life, but while they left home on their own, they tended to remain within the neighborhood. Those in ADL-3 (n=20) were almost independent within their homes; they did not stay in bed during the day, but needed assistance to leave home. Those in ADL-4 (n=4) were slightly less independent within their homes; these subjects sometimes stayed in bed during the day, left home infrequently, and required assistance when they did go out. Those in ADL-5 (n=2) needed some assistance indoors, and although they could walk on their own, they mainly stayed in bed during the day. Those in ADL-6 (n=1) spent the entire day in bed and needed assistance to eat, change clothes, a use the toilet. This classification was based on the ADL standards provided by the Ministry of Health, Labour and Welfare of Japan. In the following analyses, we regarded the subjects with ADL-1 and ADL-2 as independent and the others as dependent. All subjects except those who lived in two cities (Buzen City and Yukuhashi City; 183 subjects) were questioned as to any medications they were currently taking. Subjects were considered to have a history of chronic disease or of cardiovascular disease based on the results of the interview. The cardiovascular diseases included cerebrovascular diseases, ischemic heart diseases and arrhythmia and were assessed without regard to whether or not a subject was being treated for hypertension.

The chronic diseases included chronic obstructive pulmonary diseases, rheumatoid arthritis, chronic gastritis, chronic hepatitis, diabetes, thyroid diseases, gout/hyperuricemia, and history of malignancies. The treatment of hypertension was defined based on the results of the interview and the subject's current medications, and was assessed independently of the baseline blood pressure at the examination. Serum glucose, total protein, total cholesterol, triglycerides, and creatinine concentration were measured. Height and weight were measured, and the body mass index (BMI) was calculated. BMI was defined as weight (in kg) divided by height^2 (in m^2). The subjects were kept in a sitting position for at least 10 min in a quiet room, and then sitting BP was measured by an oscillometric method using an automatic device (BP-103; Nippon Colin, Komaki, Japan). BP measurements were performed once for each subject using a similar technique. The subjects were divided into three groups according to their systolic BP (SBP): below 140 mmHg (group 1), 140 to 159 mmHg (group 2), and 160 mmHg or over (group 3). The classification of SBP was based on the Japanese Society of Hypertension Guidelines for the Management of Hypertension. Group 2 corresponds to mild hypertension and group 3 corresponds to moderate or severe hypertension (*15*).

Data Analysis

All data were expressed as the means±SD and analyzed using SSPE for Windows, version 12.0 (SPSS Inc., Chicago, USA). One-way ANOVA or χ^2 tests were used to compare data between groups. Comparisons of the survival rates among the

Table 1. Baseline Characteristics of the Subjects in the 8020 Project

	Total	Group 1 (<140 mmHg)	Group 2 (140–159 mmHg)	Group 3 (≥160 mmHg)	*p*
Number	639	212	217	210	
Male/female	256/383	85/127	94/123	77/133	0.375
Height (m)	1.50±0.09	1.49±0.10	1.50±0.08	1.50±0.08	0.562
Weight (kg)	51.0±9.3	49.2±8.7	51.1±9.2	53.0±9.7	<0.001**
BMI (kg/m^2)	22.7±3.3	22.1±3.2	22.6±3.0	23.5±3.6	<0.001**
SBP (mmHg)	151±23	126±11	150±5	176±15	<0.001**
DBP (mmHg)	79±12	69±8	79±8	89±11	<0.001**
Heart rate (bpm)	70±12	70±12	71±13	71±11	0.655
Treatment of hypertension (%)	36.0	27.4	36.4	44.3	0.001**
History of cardiovascular diseases (%)	22.7	25.0	24.0	19.0	0.297
Smoking habit (%)	13.3	15.1	12.0	12.4	0.593
ADL (ratio of dependent ADL) (%)	4.4	6.6	3.2	3.3	0.148
Total protein (g/dL)	7.3±0.5	7.2±0.5	7.3±0.4	7.5±0.5	<0.001**
Creatinine (mg/dL)	1.0±0.4	1.0±0.2	1.0±0.2	1.0±0.6	0.499
Total cholesterol (mg/dL)	206±37	201±37	206±35	211±40	0.024*
Triglycerides (mg/dL)	119±62	111±50	119±62	129±70	0.019*
Glucose (mg/dL)	121±51	121±52	121±51	121±49	0.991

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; ADL, ability of daily life. *$p<0.05$, **$p<0.01$. Conversion factors to SI units for creatinine, total cholesterol, triglycerides and glucose were 76.25, 0.02586, 0.01120 and 0.5551, respectively.

BP categories were made using the method of Kaplan and Meier. The base Cox proportional hazards regression model was adjusted for living district, gender (male/female), BMI, heart rate, smoking habit (current smoker/noncurrent smoker), ADL (independent/dependent), total protein, total cholesterol, and triglycerides. To assess the associations between SBP or diastolic BP (DBP) category and 4-year mortality, the model was adjusted for the covariates described above, as well as DBP or SBP, respectively. In the subgroup analysis of the subjects with a history of cardiovascular disease, the model was adjusted for covariates described above, as well as DBP and SBP category. In the subgroup analysis of the subjects who were being treated for hypertension, 183 of 639 subjects who were not properly questioned in regard to their medications were excluded from the analysis, and model was included covariates described above, as well as DBP and SBP category. Values of $p<0.05$ were considered to indicate statistical significance.

Results

Table 1 shows the baseline characteristics of each of the three groups defined by SBP levels. Body weight, BMI, DBP, total protein, total cholesterol, and triglycerides in group 3 were significantly higher than those in group 1. The number of subjects who were taking antihypertensive medication increased with increasing SBP level. During the 4-year follow-up period, 87 individuals (46 males and 41 females) died. Because the total mortality of males was significantly higher than that of females, Kaplan and Meier survival curves were drawn separately for each gender. Of these deaths, 24 were due to cardiovascular diseases (6 heart failure, 5 myocardial infarctions, 4 strokes, 4 aortic aneurysms, 3 ischemic heart diseases, 1 sick sinus syndrome, and 1 hypertensive heart disease; 7 males and 17 females), 25 were due to cancer, 19 were due to pneumonia, 6 were due to chronic obstructive lung diseases, 6 were due to accidents such as fire, falling, or traffic accidents, 2 were due to suicides, and 2 were due to renal failure. The causes of death for the other subjects ($n=3$) were unknown. Figure 1, which shows the survival curves for each group over the 4-year follow-up period, demonstrates that there were no significant differences in survival among the three SBP groups for total subjects or for either gender. In multivariate Cox regression analysis, total and cardiovascular mortality were also not significantly different among the groups (Table 2). However, because the mortality in group 3 was slightly higher than that of group 1, subgroup analyses were performed to investigate whether preexisting disease status may have affected the mortality in the present study. The adjustment of the chronic disease status in the Methods section did not affect the results of the analyses (data not shown). One hundred and forty-five subjects had a history of or were currently being treated for cardiovascular diseases, including 63 cases of cerebrovascular diseases, 55 cases of ischemic coronary diseases, and 35 cases of arrhythmia. Among the subjects with cardiovascular diseases, those assigned to group 3 had a significantly higher all-cause mortality than those in group 1 (Table 2). Thus cardiovascular

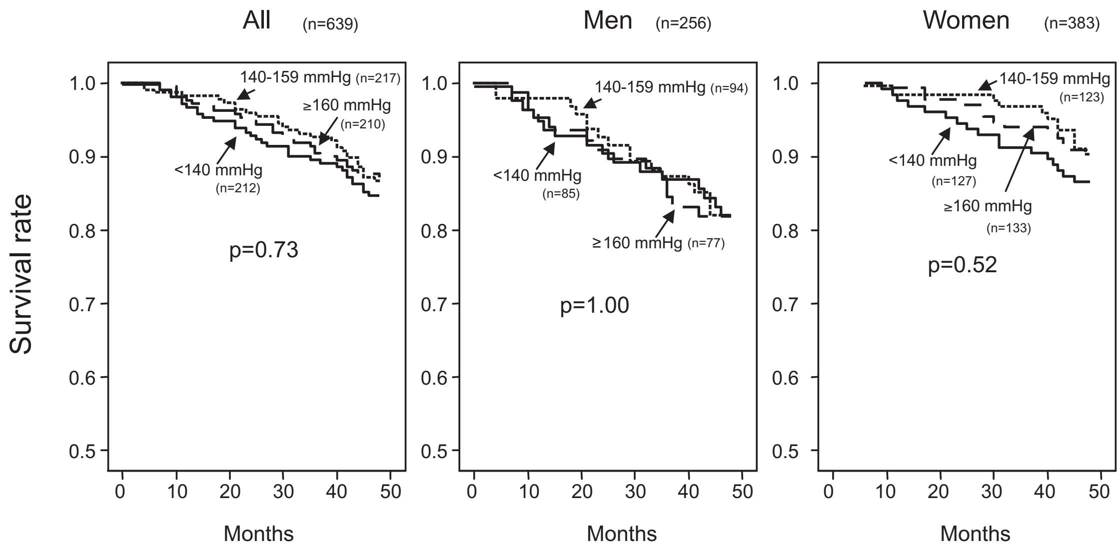

Fig. 1. *Systolic blood pressure (SBP) levels and time to death analyses using Kaplan-Meier analysis.*

Table 2. Deceased Number and Relative Risks of Total and Cardiovascular Deaths by BP Category Calculated form Multivariate Cox Proportional Hazards Models

	Deceased	BP category			*p*
	(*n*)	Group 1	Group 2	Group 3	
Total deaths					
All subjects (n=639)	87	1.00	1.23 (0.67–2.26)	1.60 (0.75–3.38)	0.46
History of cardiovascular disease					
No (n=494)	67	1.00	1.17 (0.59–2.30)	0.70 (0.28–1.79)	0.39
Yes (n=145)	20	1.00	0.79 (0.12–5.32)	11.9 (1.90–75.2)†	<0.01
Treatment of hypertension					
No (n=290)	43	1.00	1.07 (0.46–2.50)	0.94 (0.27–3.28)	0.96
Yes (n=166)	19	1.00	1.04 (0.19–5.69)	5.98 (1.01–48.4)†	0.03
Cardiovascular deaths					
All subjects (n=639)	24	1.00	1.71 (0.56–5.24)	2.15 (0.51–8.97)	0.54
History of cardiovascular disease					
No (n=494)	17	1.00	1.93 (0.48–7.67)	1.62 (0.27–9.51)	0.64
Yes (n=145)	7	1.00	3.26 (0.21–50.6)	14.0 (0.28–699)	0.40
Treatment of hypertension					
No (n=290)	9	1.00	0.85 (0.13–5.64)	0.95 (0.72–12.6)	0.98
Yes (n=166)	8	1.00	23.7 (0.96–587)	0.65 (0.11–37.6)	0.38

Relative risks are adjusted for sex, body mass index, smoking habits, ADL dependency, diastolic blood pressure, heart rate, total protein, total cholesterol, triglycerides. BP, blood pressure; ADL, ability of daily life. $^{\dagger}p<0.05$.

mortality in these subjects tended to be increased with their SBP levels. On the other hand, in the subjects without cardiovascular diseases (n=494), total and cardiovascular mortality were almost the same among the groups. To analyze the effects of treatment of hypertension on the mortality in this population, we enrolled 456 subjects whose medical history and medications were completely clarified (Table 2). In the subjects receiving treatment for hypertension (n=166), multivariate Cox regression analysis revealed that all-cause mortality in group 3 was significantly higher than that in group 1. However, we did not find such a difference in the subjects who were not receiving treatment for hypertension (n=290). Because we found that males had a significantly higher mortality rate than females, we performed a Cox regression analysis after adjustment for gender. However, there was no association between SBP category and 4-year mortality (RR 0.78, CI 0.49–1.29, group 3 compared with group 1, p=0.45). Furthermore, we analyzed using several other models adjusted with different factors, but we could not find different results. As several previous studies included a group with a much lower SBP level than this study, we also performed subgroup analyses in which the lowest SBP group consisted of subjects whose SBP were lower than 120 mmHg ($n=68$). The risk of total death of the lowest SBP group was not significantly different compared with that of the subjects whose SBP were 120–140 mmHg ($n=144$) (RR 0.68, CI 0.29–1.59, $p=0.38$).

We also examined the relation between DBP and 4-year mortality in this population. For this analysis, subjects were divided into three groups according to their DBP: below 75 mmHg ($n=216$), 75 to 89 mmHg ($n=284$), and 90 mmHg or over ($n=104$). Cox proportional hazard regression analysis revealed that there were no associations between DBP category and 4-year mortality (RR 0.51, CI 0.15–1.02, highest DBP group compared with lowest DBP group, $p=0.11$).

Discussion

The present study demonstrated that the SBP levels in 80-year-old subjects were not associated with total and cardiovascular mortality during a 4-year–observation period in a general Japanese population. An exception to this was seen in the subset of subjects with cardiovascular diseases and/or receiving treatment for hypertension, among whom significantly higher total mortality was seen with increasing SBP.

Because the average duration of life for an 80-year-old in Japan in 1997 was 7.56 for men and 10.08 for women (*14*), most of the very elderly will still require healthcare for at least five more years. Most of the previous studies on the impact of BP on mortality in the very elderly have shown worsened mortality with low BP (*2–9*). The cut-off points of SBP for increasing mortality differ among these studies, but in the present study we found no increase in mortality in subjects whose SBP values were lower than 120 mmHg. The precise mechanisms of the deleterious effect of low BP on mortality in the very elderly are not clear, but some authors speculated that preexistent diseases such as cancer, cardiovascular diseases (*4*, *12*), pulmonary diseases (*4*), and dementia (*6*, *7*) lowered BP and increased the mortality in the very elderly. In the present study, because the data collection was performed at a healthcare center or public hall, almost all participants were able to walk independently. Furthermore, we did not include subjects living in nursing homes, and 96% of participants were classified as independent based on their ADL (Table 1). The death rate per 1,000 persons in the present study was 34.4, which was much smaller than that for 80- to 84-year-old individuals in the overall Japanese population in 2000 (56.4 deaths/1,000 persons) (*14*). Participants in the present study were thus relatively “healthy” elderly. Accordingly, the lower SBP did not increase the mortality in the present survey. Because the ratio of cardiovascular mortality at the age of 80 based on the death statistics in Japan is about 30% (*14*) and almost equal to that in the present study ($24/87=0.27$), there was no apparent selection bias in the subjects of this survey.

Although Japan has one of the longest life expectancies in the world, only one study has been conducted to analyze the relation between BP and mortality (*13*) in this country. The study demonstrated that an increase in total mortality was observed in both the lowest and highest BP groups in the elderly (mean age, 73.5 years). Furthermore, a linear association was observed between SBP and cardiovascular mortality. The results of the present study and this former study (*13*) in Japan were different from those of other previous studies (*2–9*). We do not know the precise mechanism responsible for this discrepancy. Stroke occurs more frequently in Japan than in most Western countries, and its morbidity is strongly associated with high BP (*16*). A difference in the morbidity of stroke and other cardiovascular diseases between Asians and Caucasians might be involved in the discrepant results between these studies.

The effects of treatment of hypertension in the very elderly are still controversial. In their guidelines, the Japanese Society of Hypertension recommended that SBP should be controlled to below 140 mmHg in elderly patients (*15*). A meta-analysis of the randomized controlled trials in subjects 80 years old and over showed that the treatment of hypertension significantly decreased strokes, cardiovascular events, and the onset of heart failure, but it reported that total and cardiovascular mortality were slightly but not significantly higher in the treatment group than the non-treatment group (*17*). The Hisayama study, one of the famous cohort studies in Japan, showed a significant elevation of the cardiovascular events in subjects over 80 years old only in the subgroup with an SBP over 180 mmHg or DBP over 110 mmHg (*18*). There has been only one randomized controlled trial conducted to determine the risks and benefits of the treatment of hypertension in patients over 80 years old, which was called the Hypertension in the Very Elderly Trial (HYVET) (*19*). The results of the pilot study for HYVET showed a significant reduction of stroke morbidity, but it also mentioned the possibility of excess deaths with active treatment. In the present study, subjects in group 3 had the highest prevalence of treatment for hypertension. Therefore, it might be possible that the treatment itself increased mortality in this subgroup. In the Systolic Hypertension in the Elderly Program (SHEP), diuretics increased the rate of cardiovascular events in subjects with hypokalemia (*20*). Because this study was a cross-sectional and observational study and medications were not controlled, it is very difficult to disentangle this problem.

In contrast, in the subjects without cardiovascular diseases or treatment of hypertension, there was no association between mortality and SBP. Because the high SBP did not increase the mortality in these subjects, physicians might not need to start new antihypertensive therapy in patients 80 years or older. However, because cardiovascular events, when not fatal, can still worsen the ADL, we should consider the effect of hypertension treatment on cardiovascular morbidity in the elderly.

Study Limitation and Perspective

The small number of total deaths and cardiovascular deaths in the present study might have been insufficient to detect differences in the total population, and as we mentioned above we did not examine the morbidity of the cardiovascular diseases. Hence further investigations, especially randomized controlled trials, will be needed to assess the effects of antihypertensive treatment on mortality and morbidity in the very elderly.

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